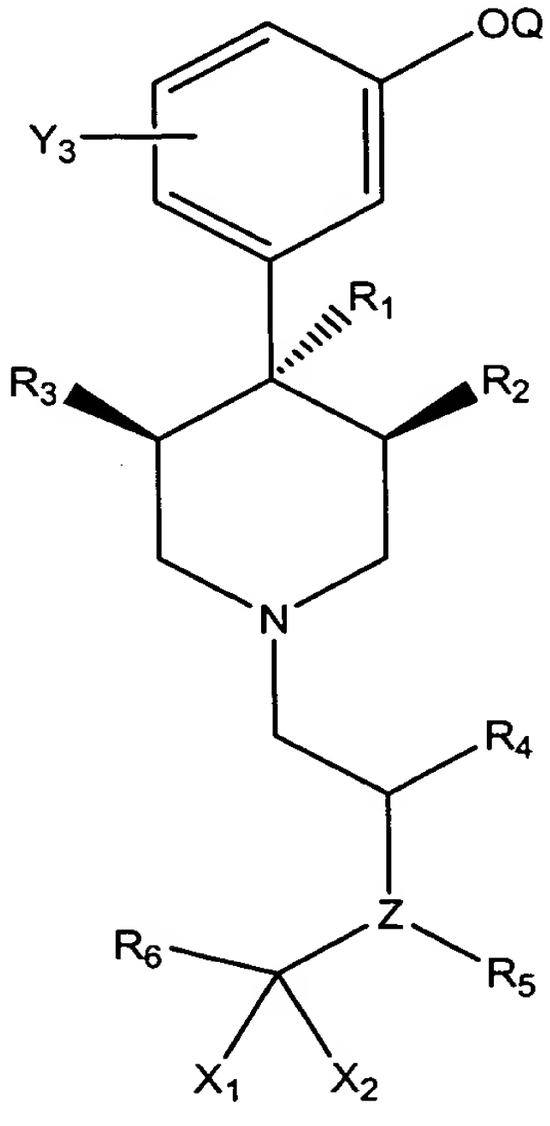
CLAIMS

Please amend the claims as follows:

Claim 1 (Previously Presented): A method of binding a kappa opioid receptor in a subject in need thereof, comprising:

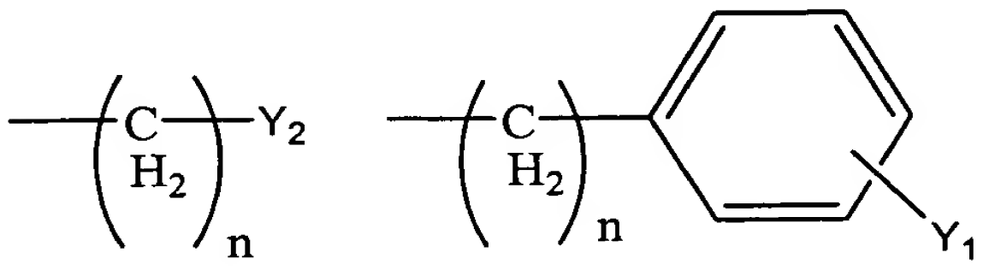
administering to said subject a composition comprising a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (1):

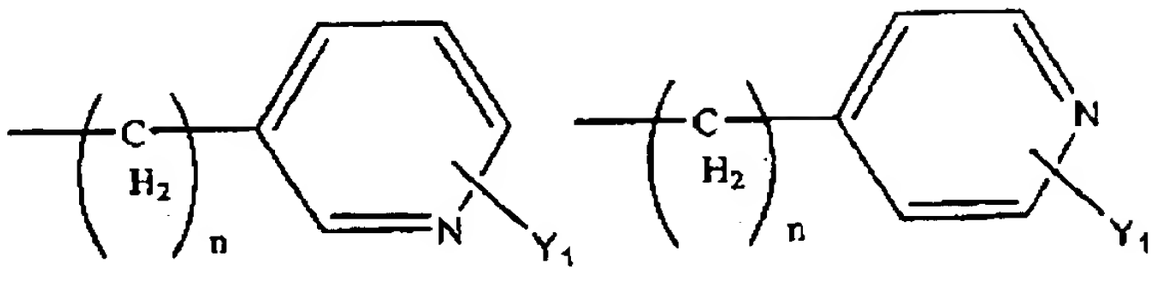


(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:





Y_1, is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3, CO_2R_9, C_{1-6}alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

wherein R_2 and R_3 may be bonded together to form a C_{2-8}, alkyl group;

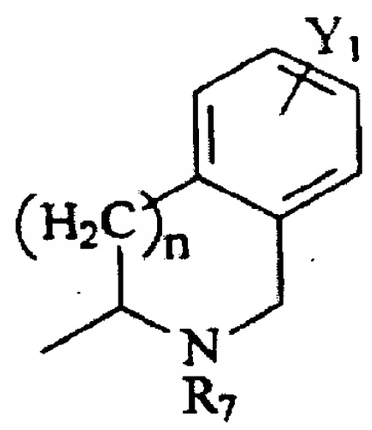
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1, CH_2aryl substituted by one or more groups Y_1 or CO_2C_{1-8} alkyl;

Z is N, O or S; where Z is O or S, there is no R_5

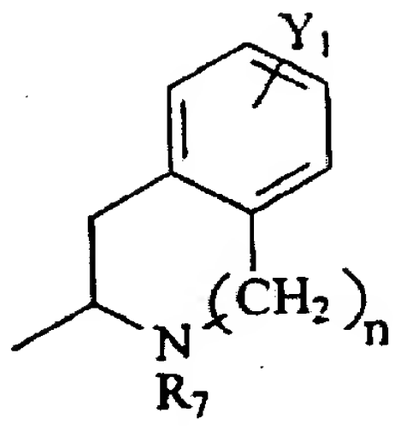
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2aryl substituted by one or more groups Y_1;

n is 0, 1, 2 or 3;

R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



(a)



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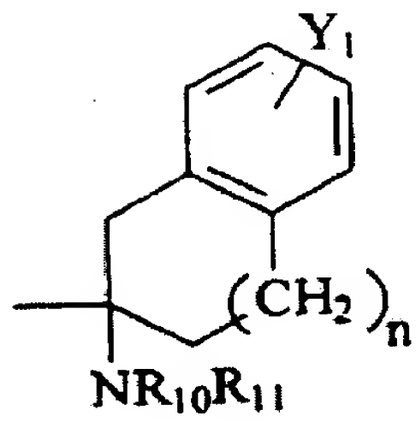

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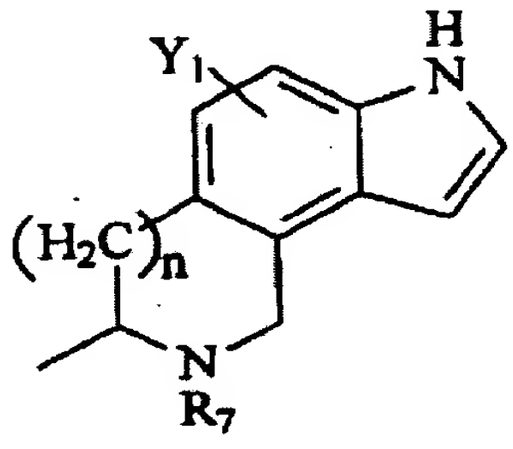

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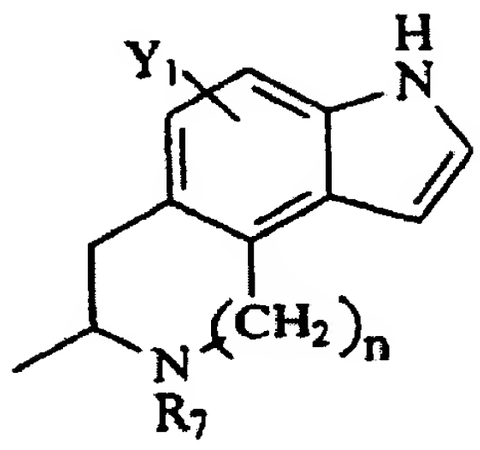

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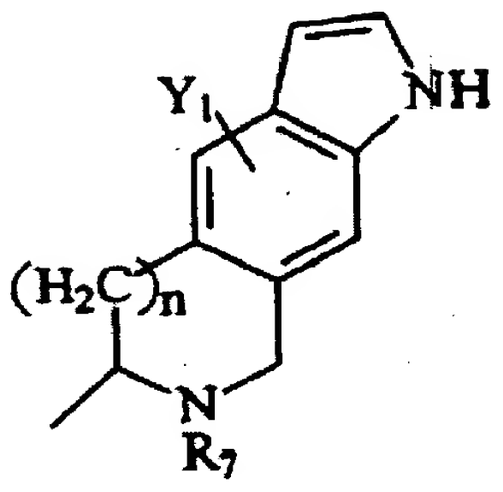

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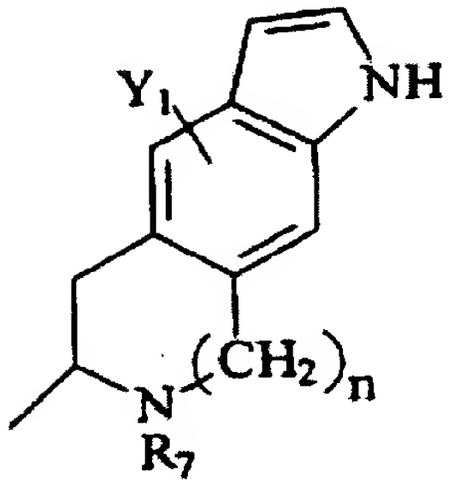

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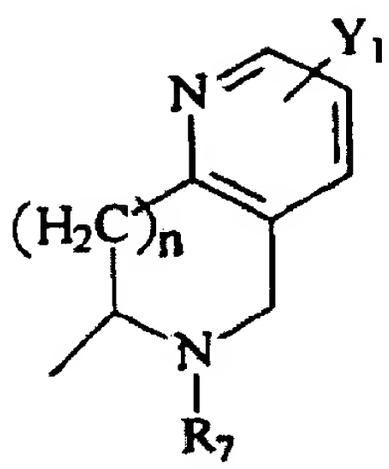

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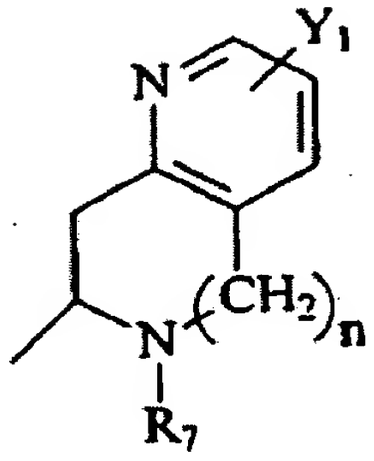

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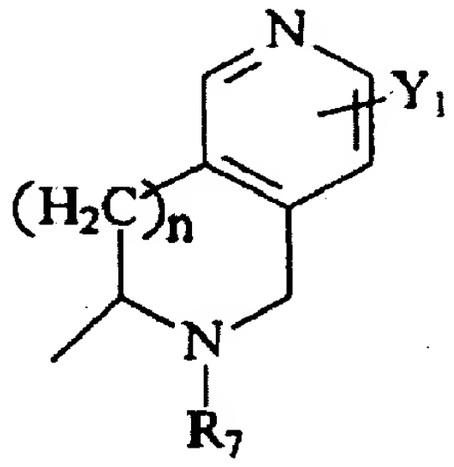

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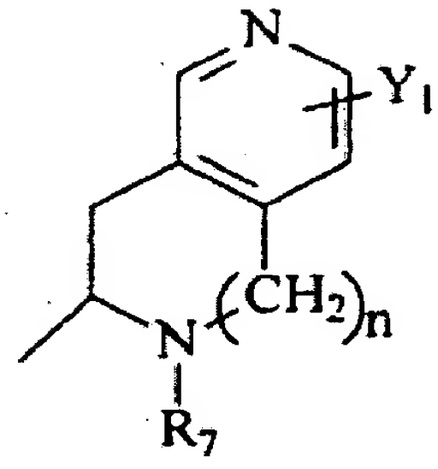

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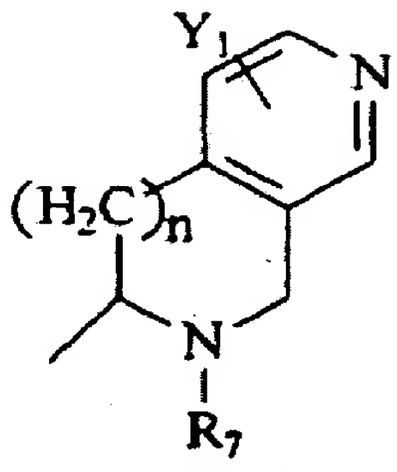

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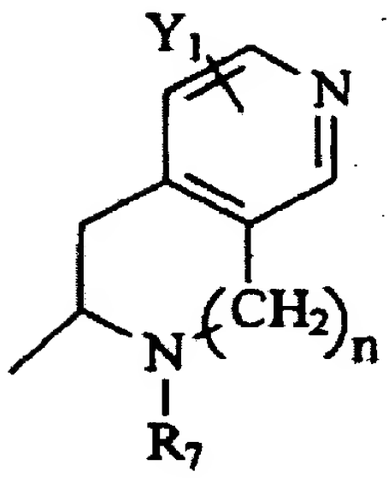

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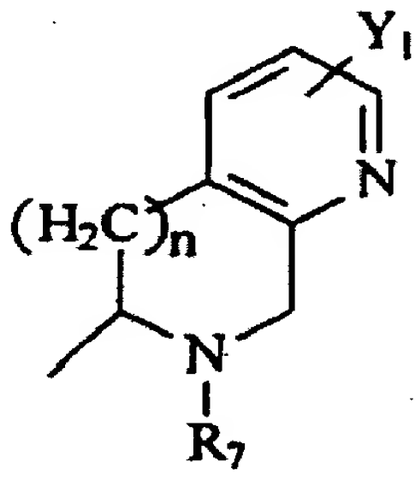

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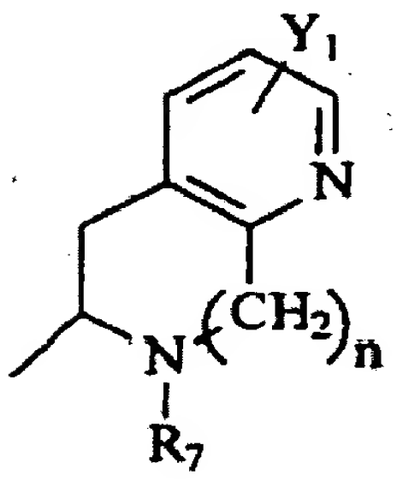

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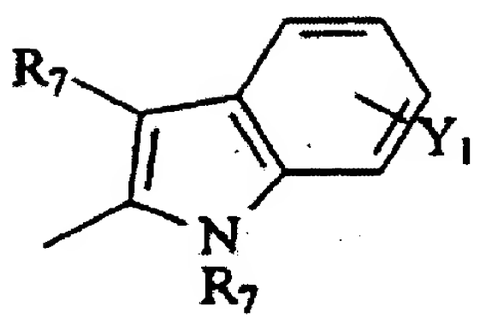

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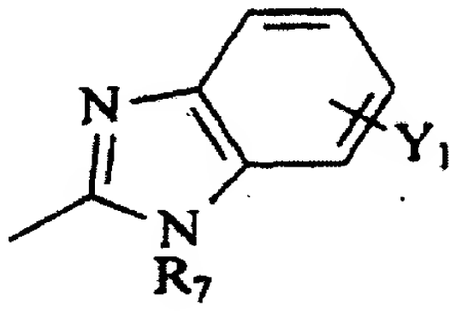

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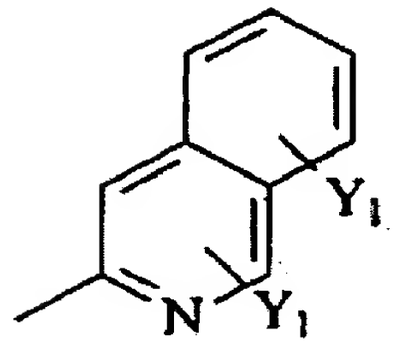

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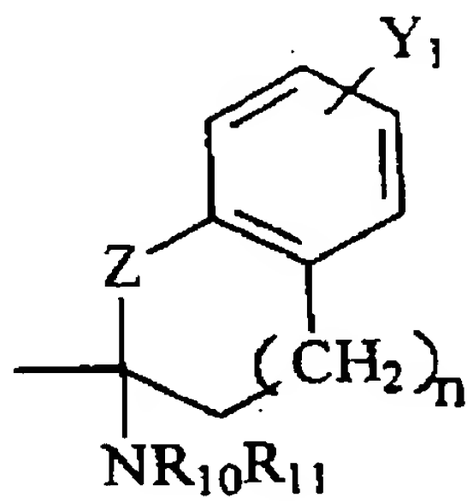

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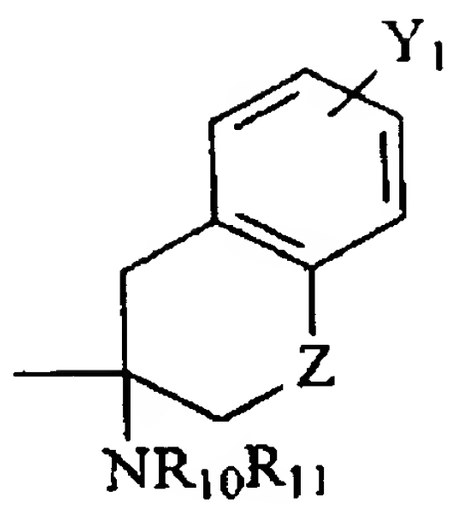

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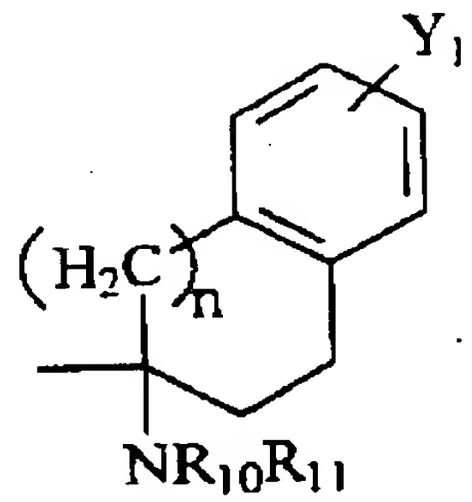

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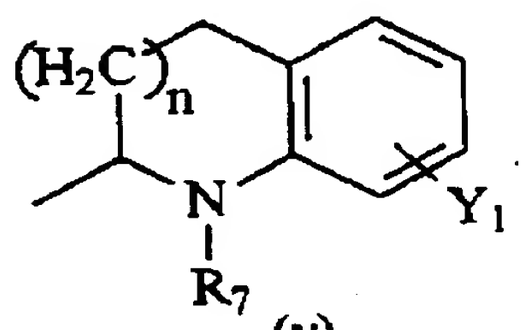

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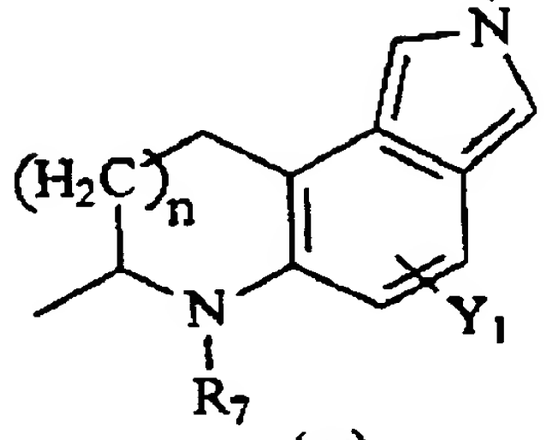

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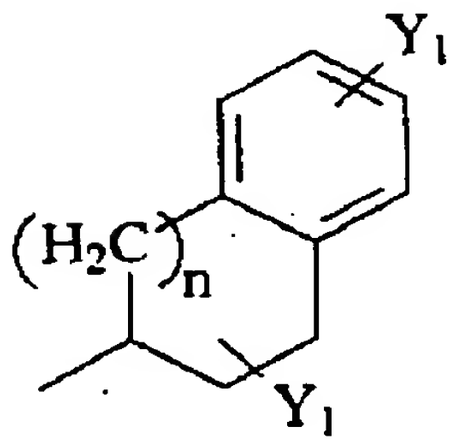

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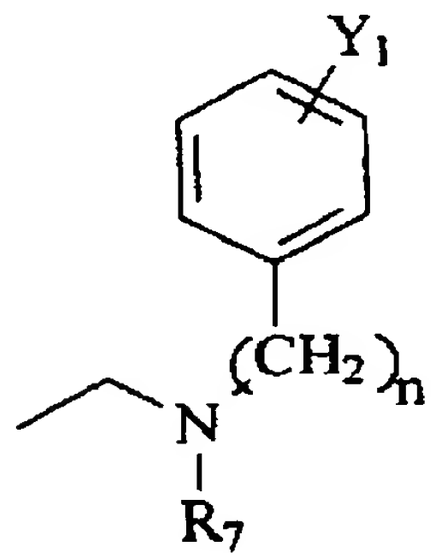

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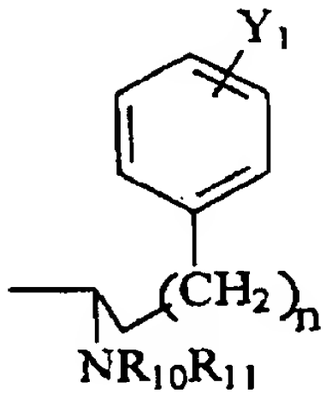

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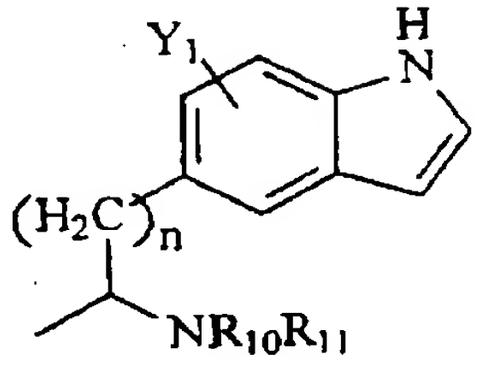

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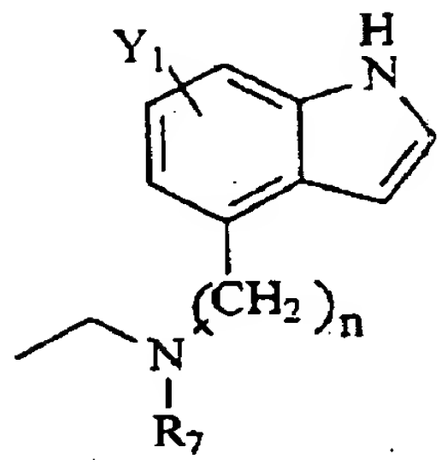

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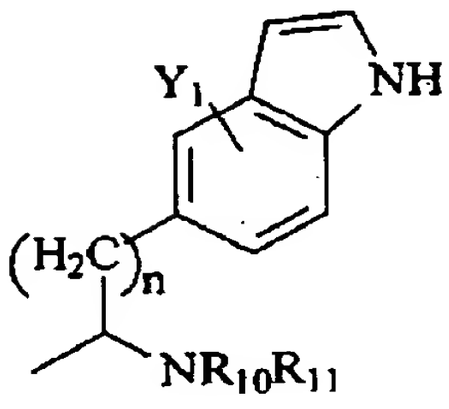

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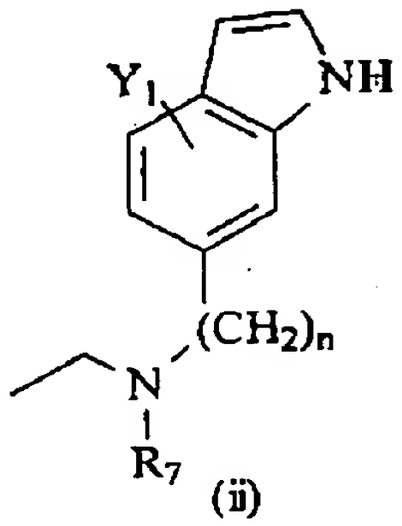

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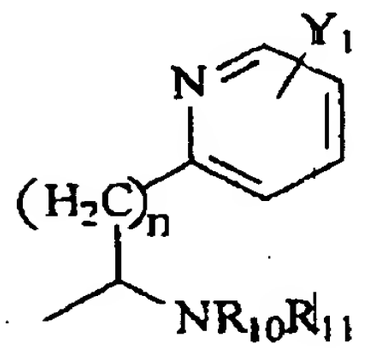

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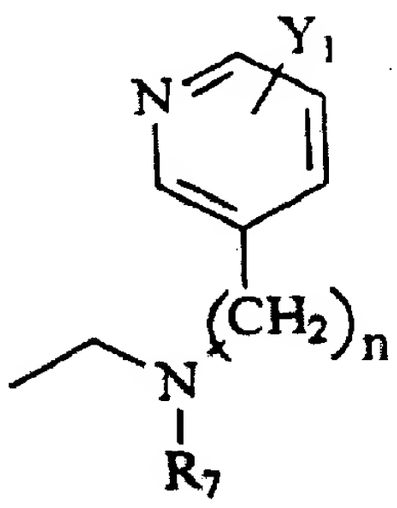

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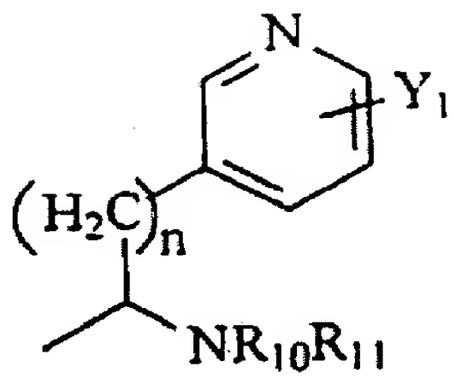

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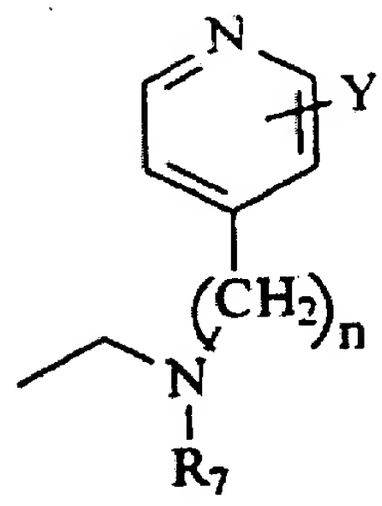

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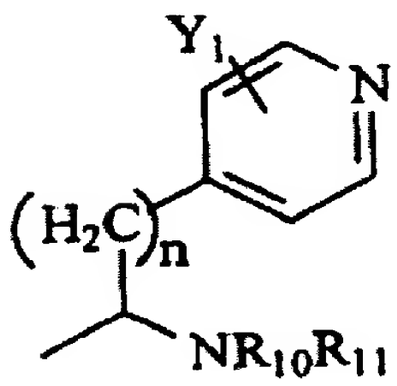

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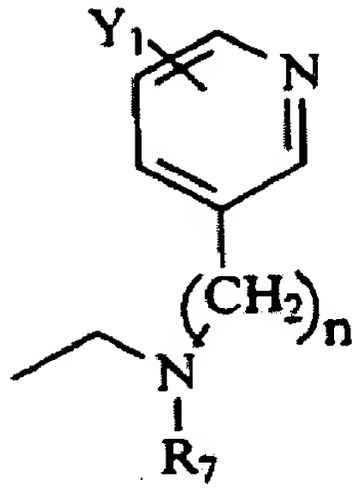

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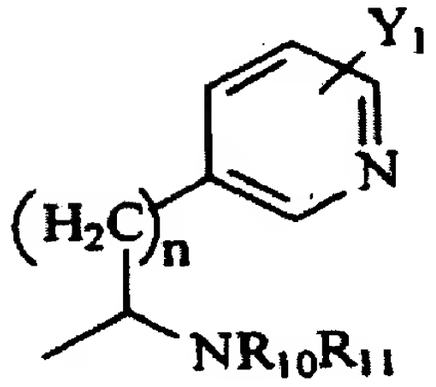

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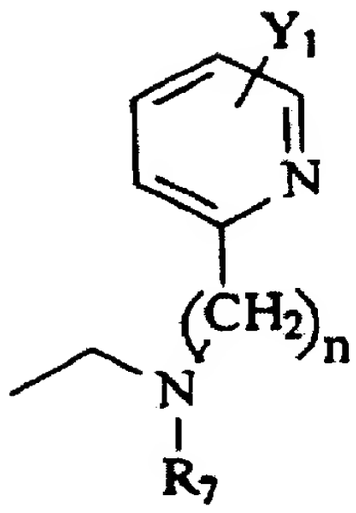

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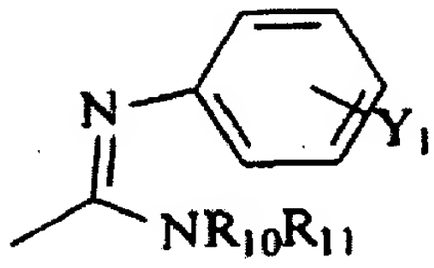

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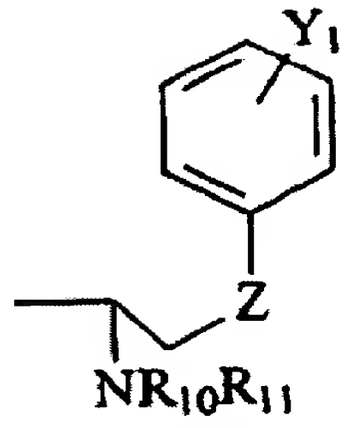

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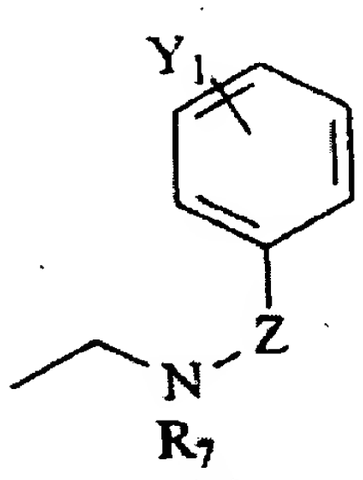
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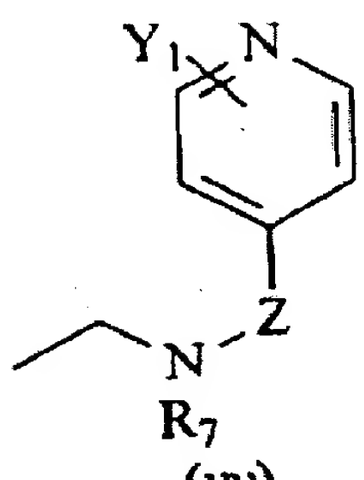
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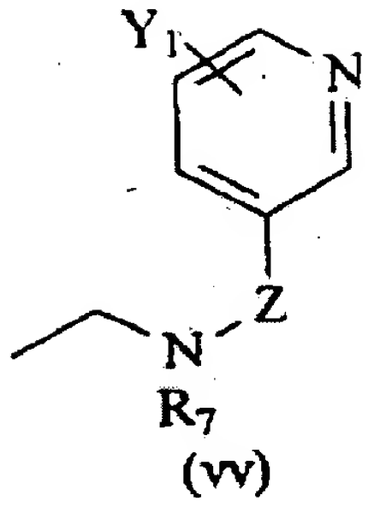
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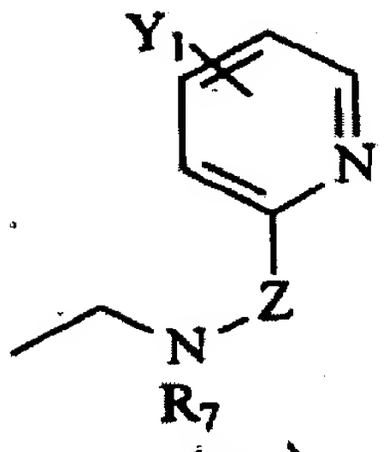
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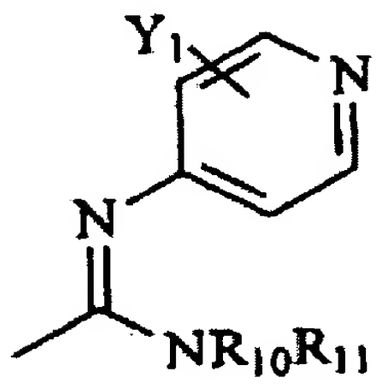
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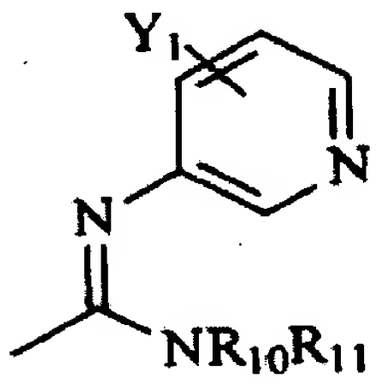
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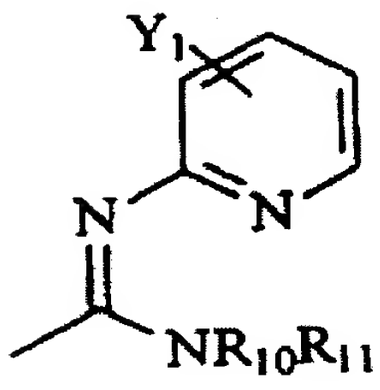
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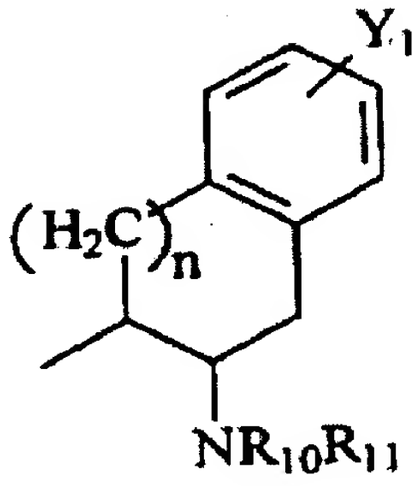
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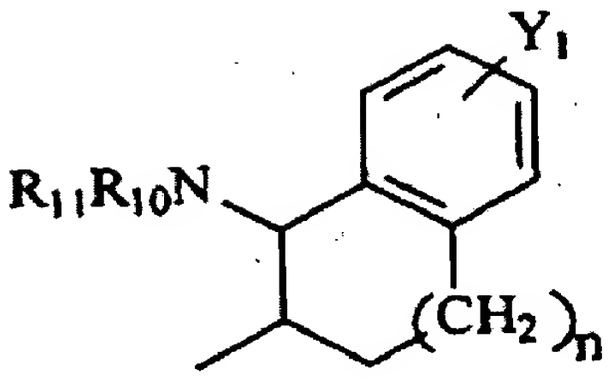

(bbb)

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

X_2 is hydrogen, C_{1-8}alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl; or

X_1 and X_2 together form =O, =S, =NH;

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, NR_{10}, R_{11}, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8}alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

and pharmaceutically acceptable salts thereof.

Claim 2 (Previously Presented): The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1, R_4, R_5, Y_1, Y_2, Z, n, X_1, X_2, and R_7-R_{17} are as in Claim 1;

Y_3 is H;

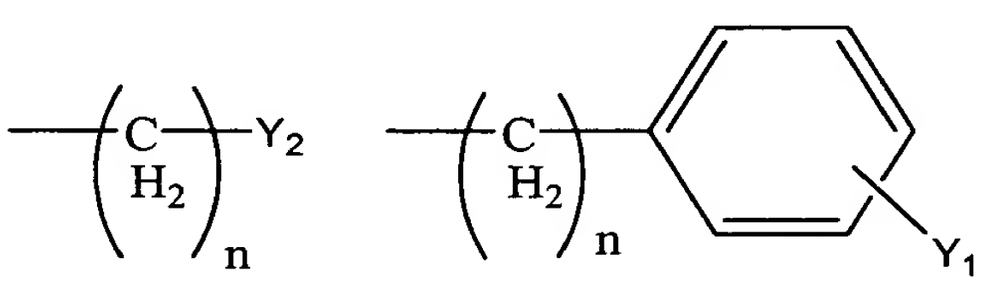
R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkynyl, C_{3-8} alkynyl, or CH_2aryl substituted by one or more substituents Y_1; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc);

and pharmaceutically acceptable salts thereof.

3. (Previously Presented) The method of claim l, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1, Y_2, R_4, R_5, Z, n, X_1, X_2 and R_8-R_{15} are as in Claim 1;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 4 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I) wherein Y_1, Z, n, X_1, X_2 and R_8-R_{15} are as in Claim 1;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8}alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, or $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 5 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound of formula (I),wherein Y_1, Z, n, X_1, X_2 and R_8-R_{14} are as in Claim 1;

R_1 is methyl,

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCO_2R_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

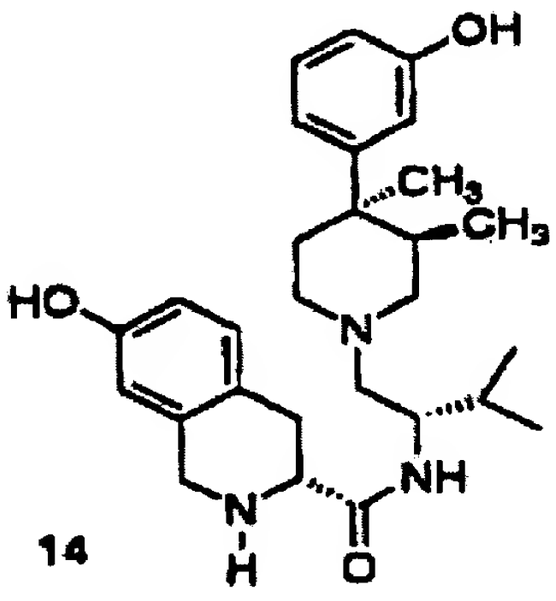
R_4 is $C_{1\text{-}8}$ alkyl, or $CO_2C_{1\text{-}8}$ alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, $C_{1\text{-}8}$ alkyl, CH_2 aryl substituted by one or more substituents Y_1, or $CH_2(CH_2)_nY_2$.

Claim 6 (Previously Presented) The method of claim 1, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 as follows:



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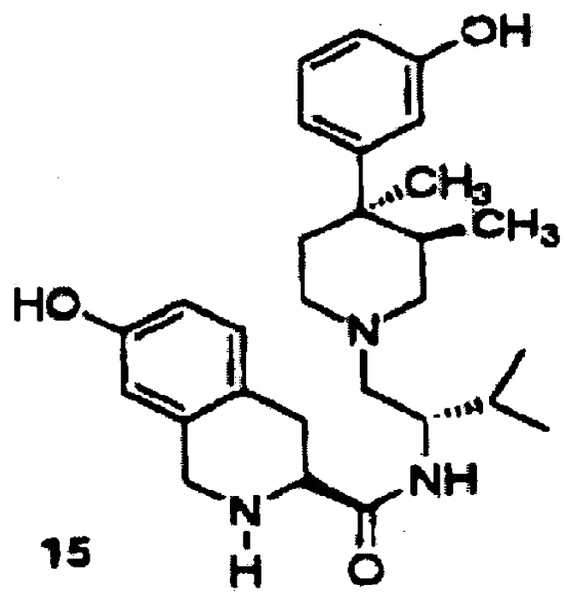

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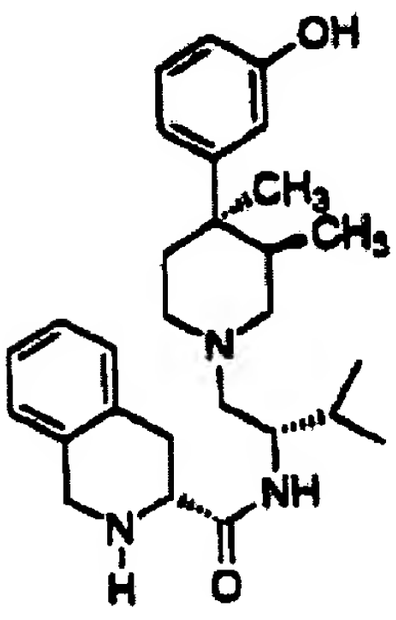

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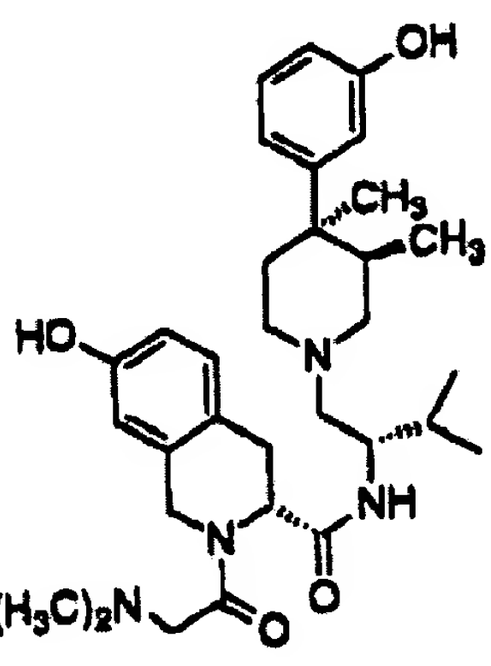

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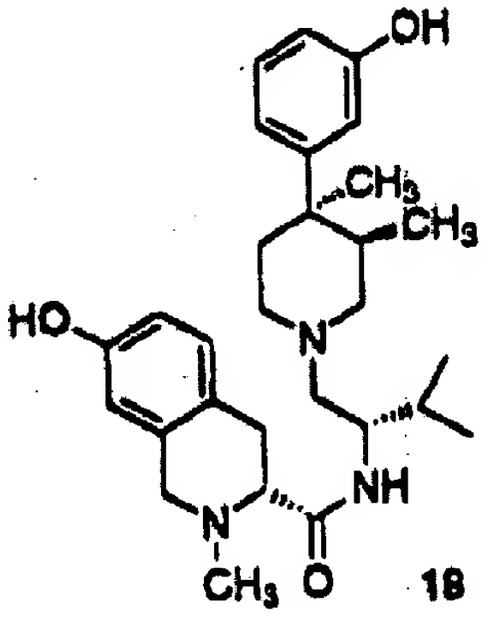

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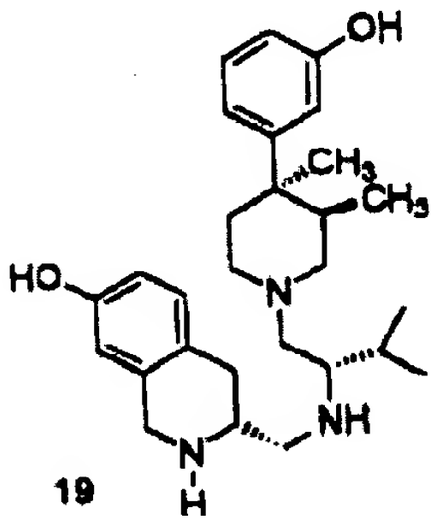

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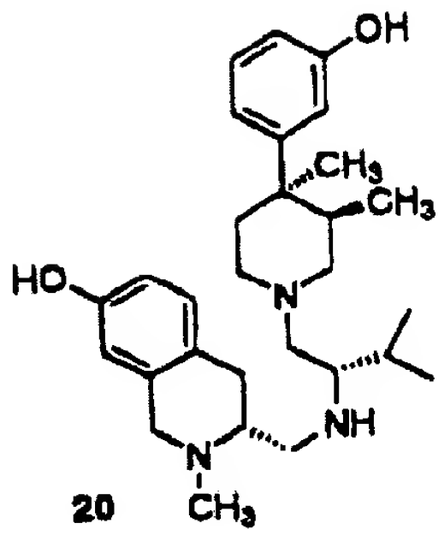

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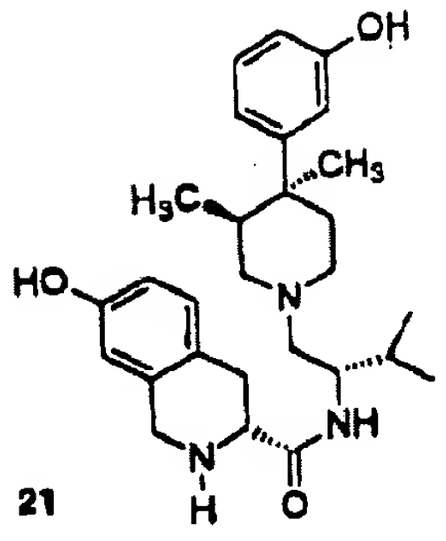
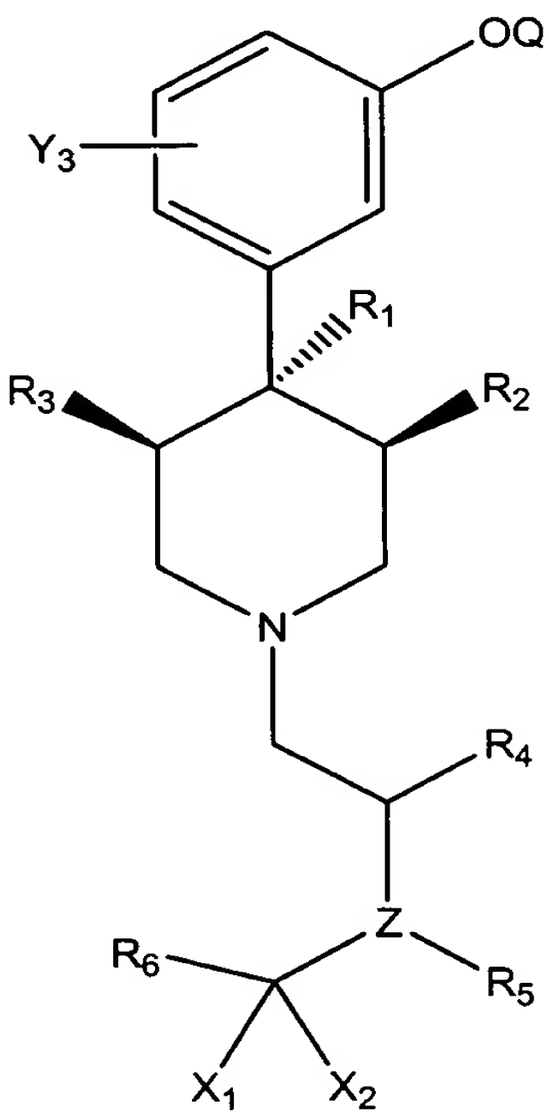


21

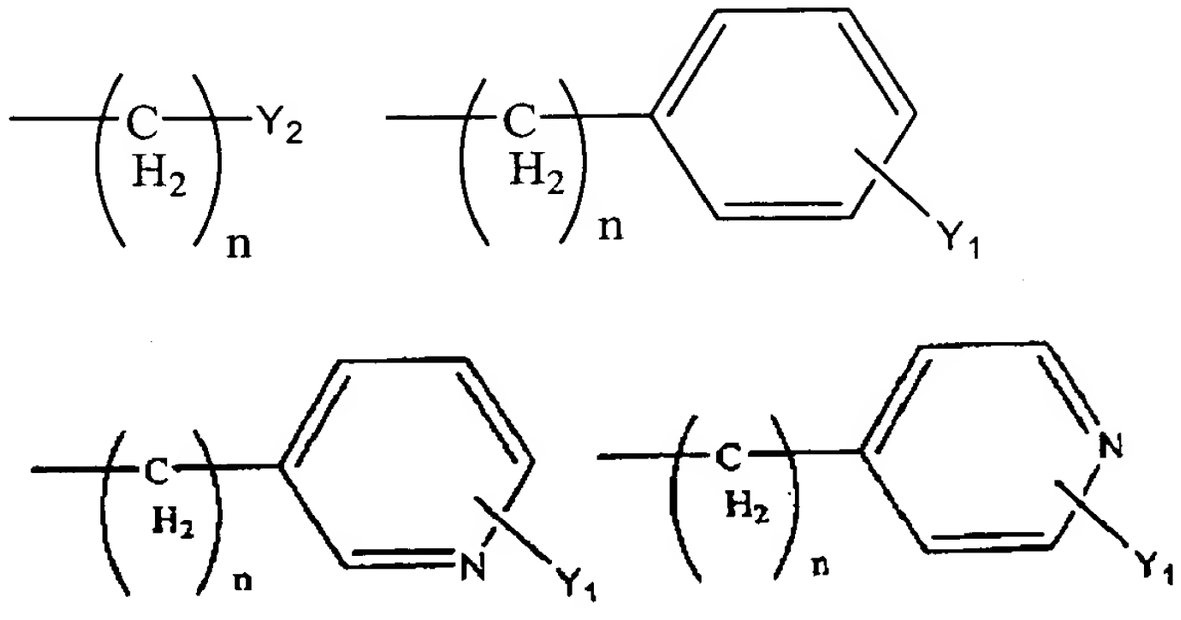
Claim 7 (Previously Presented) A kappa opioid receptor antagonist compound represented by the formula (I):



(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, $C0_2R_9$, $C_{1\text{-}6}$ alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY_2$;

Y_2 is H, CF_3, CO_2R_9, $C_{1\text{-}6}$alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_3R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, $C_{1\text{-}6}$ alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or CH2$(CH_2)_nY_2$;

R_2 is H, $C_{1\text{-}8}$ alkyl, $C_{3\text{-}8}$alkenyl, $C_{3\text{-}8}$ alkynyl or CH_2aryl substituted by one or more groups Y_1;

R_3 is H, $C_{1\text{-}8}$ alkyl, $C_{3\text{-}8}$ alkenyl, $C_{3\text{-}8}$ alkynyl or CH_2aryl substituted by one or more groups Y_1;

wherein R_2 and R_3 may be bonded together to form a $C_{2\text{-}8}$ alkyl group;

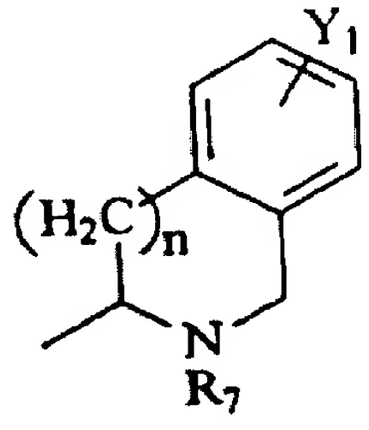
R_4 is hydrogen, $C_{1\text{-}8}$ alkyl, $CO_2C_{1\text{-}8}$ alkylaryl substituted by one or more groups Y_1, CH_2aryl substituted by one or more groups Y_1 or $CO_2C_{1\text{-}8}$ alkyl;

Z is N, O or S; when Z is O or S there is no R_5

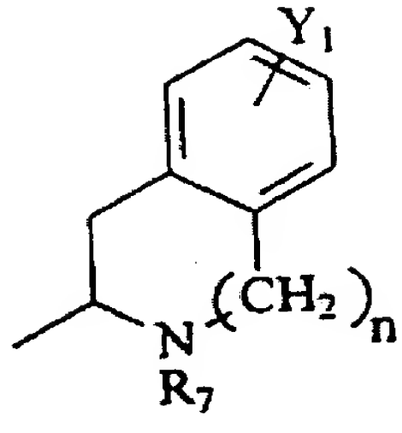
R_5 is H, $C_{1\text{-}8}$ alkyl, $C_{3\text{-}8}$ alkenyl, $C_{3\text{-}8}$ alkynyl, $CH_2CO_2C_{1\text{-}8}$ alkyl, $CO_2C_{1\text{-}8}$ alkyl or CH_2aryl substituted by one or more groups Y_1;

n is 0, 1, 2 or 3;

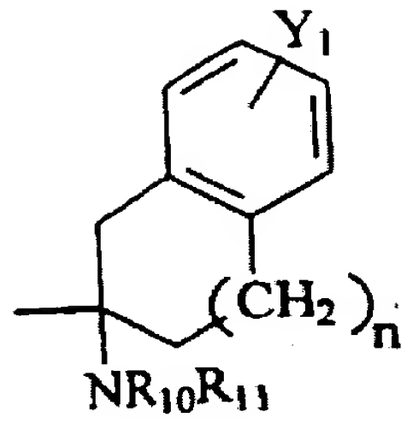
R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



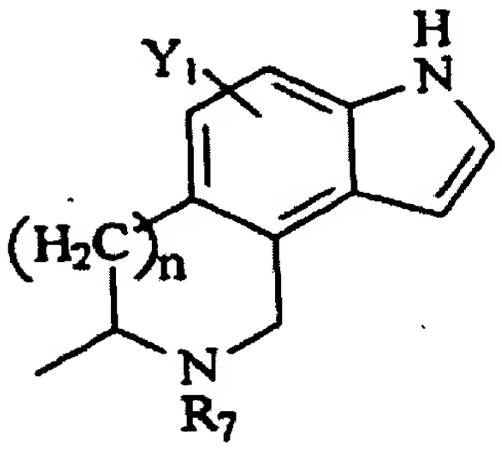
(a)



(b)



(c)



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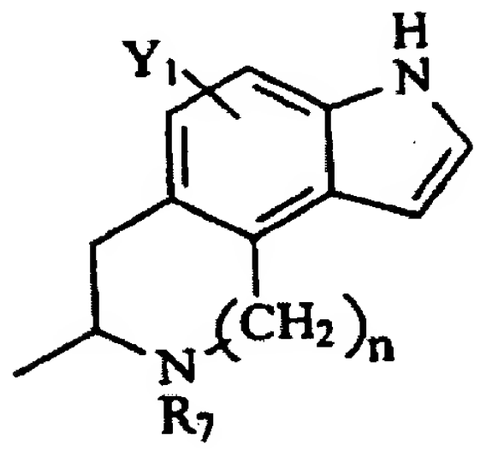

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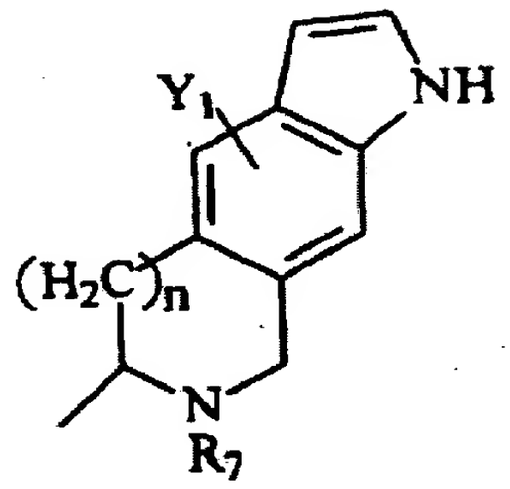

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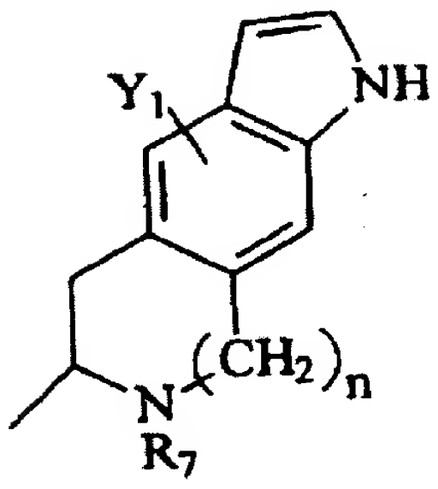
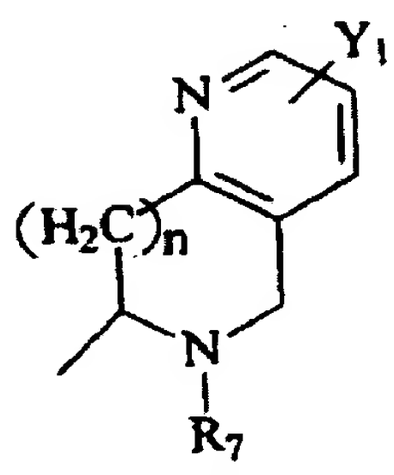
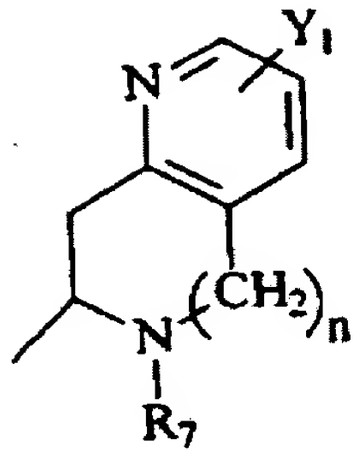


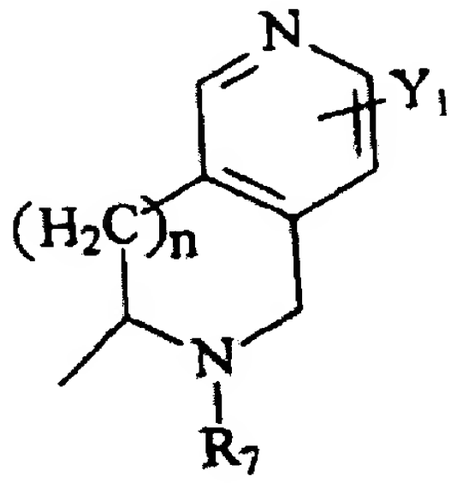
(g)



(h)



(i)



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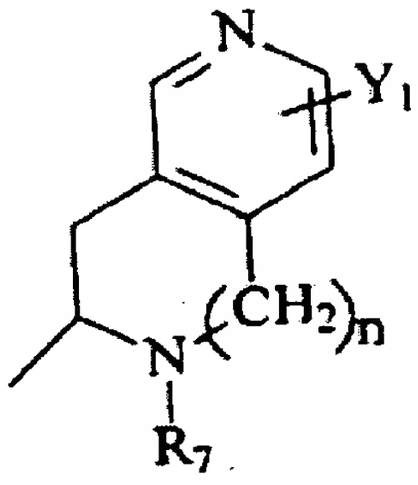

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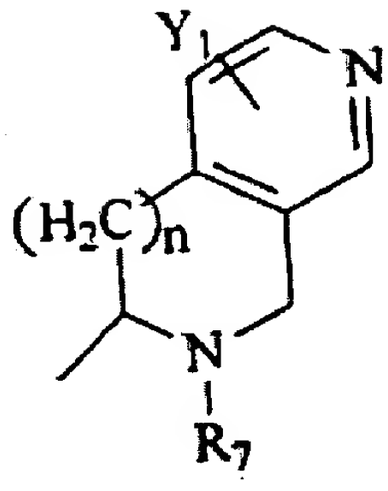

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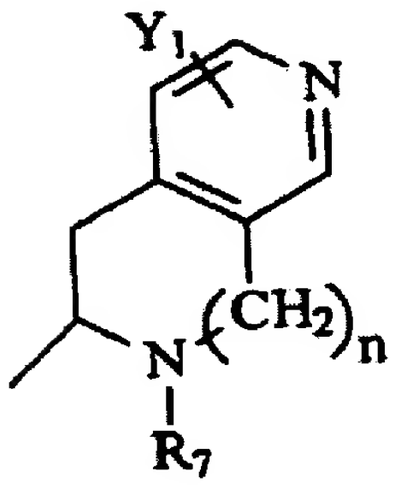

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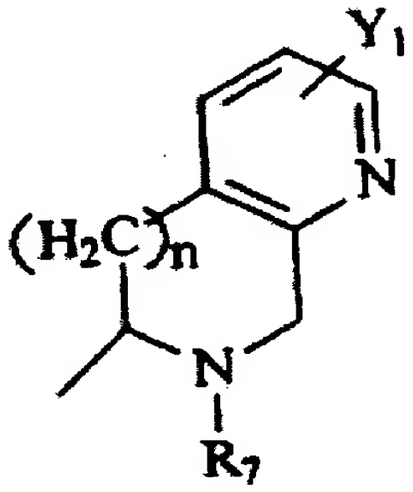

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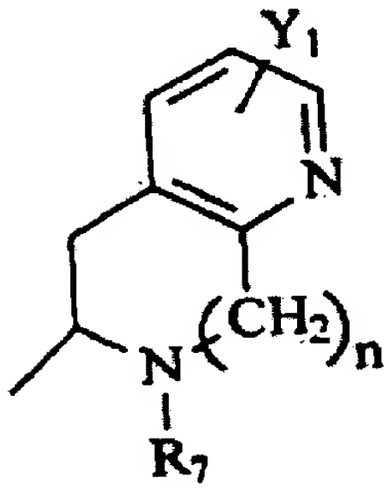

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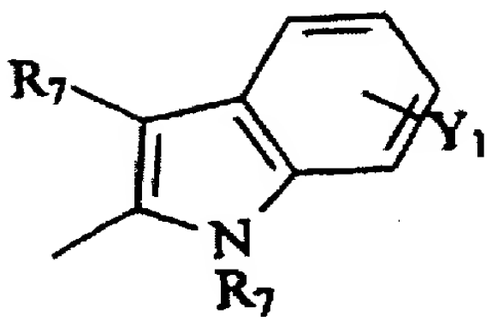

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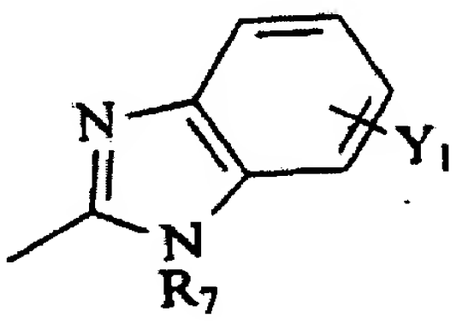

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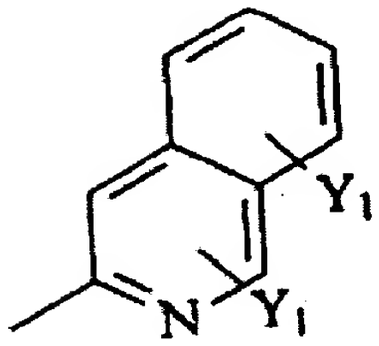

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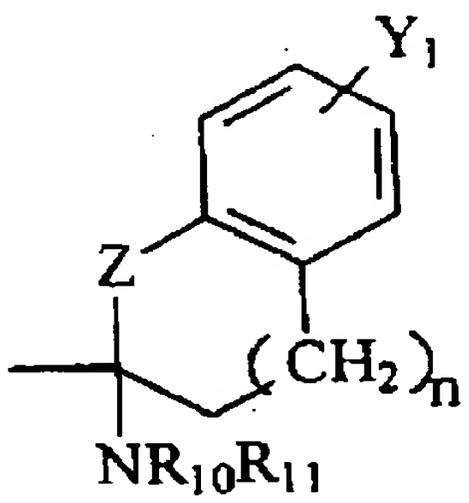

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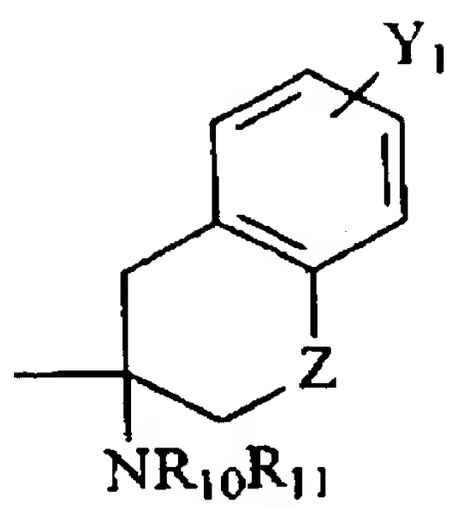

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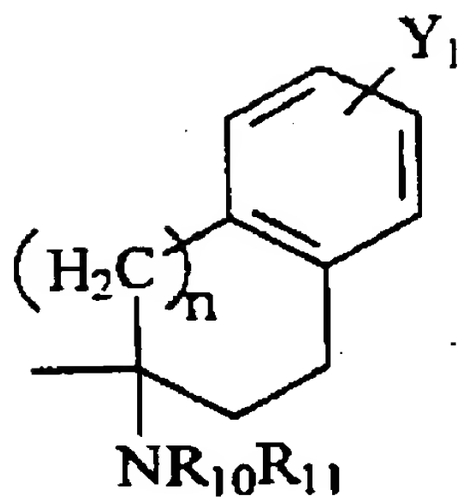

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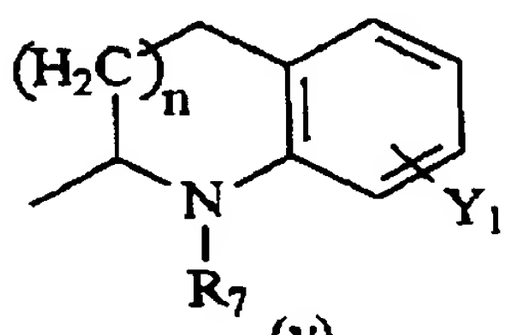

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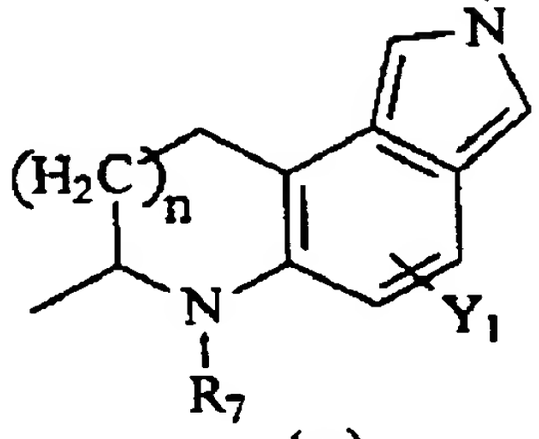

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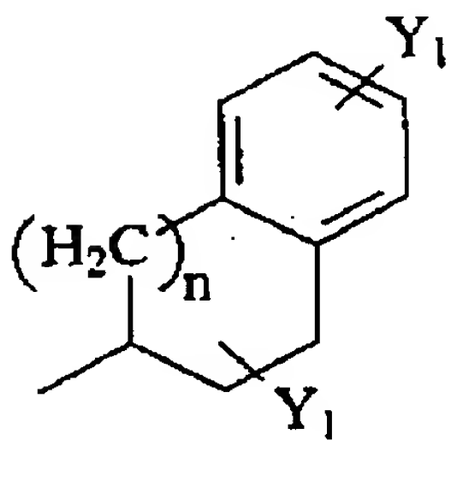

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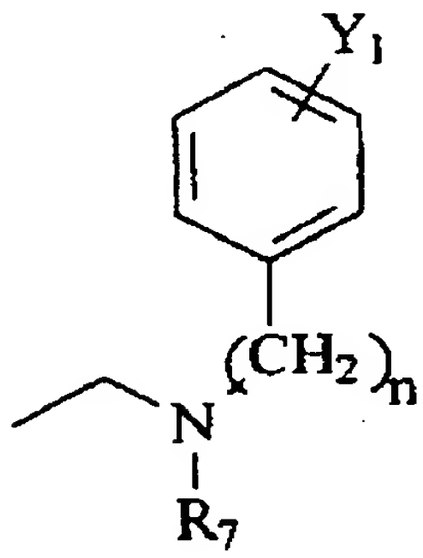

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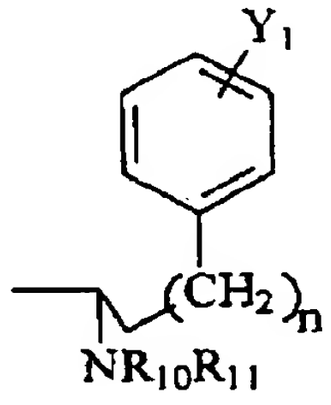

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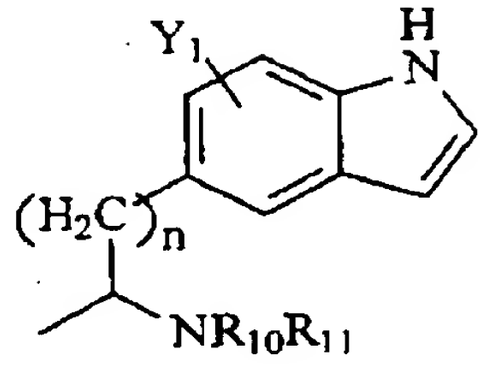

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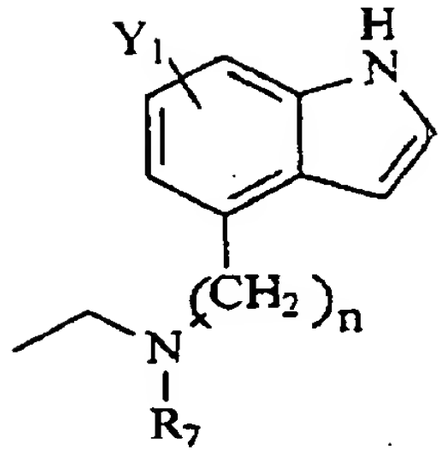

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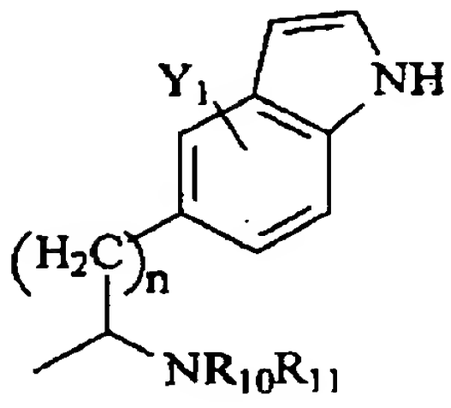

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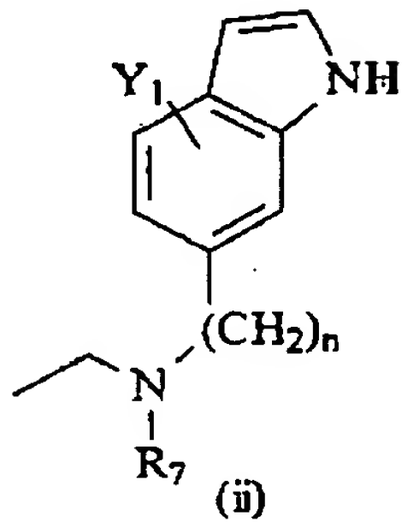

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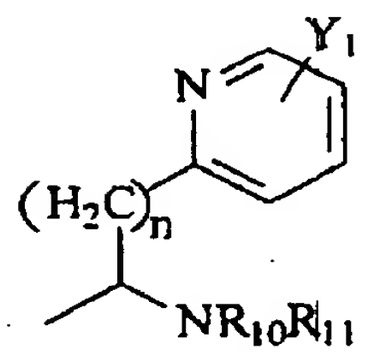

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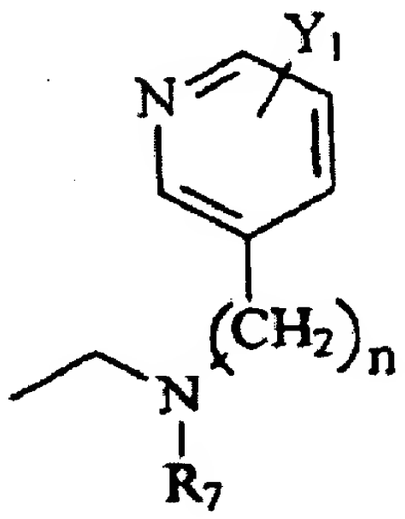

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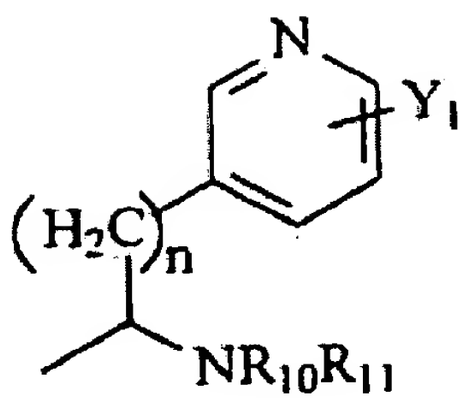

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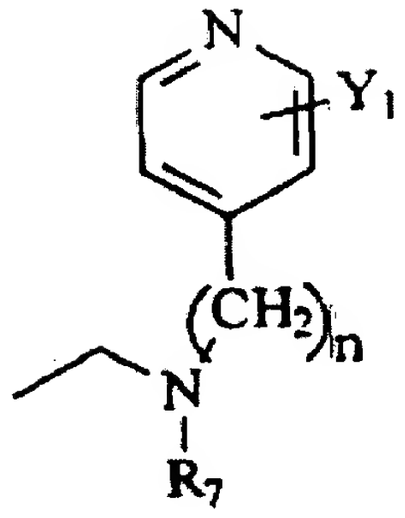

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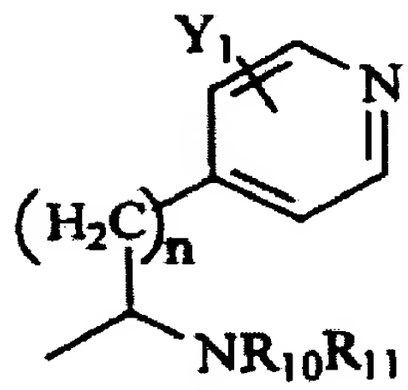

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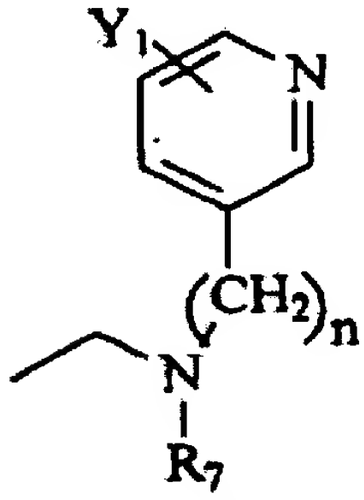

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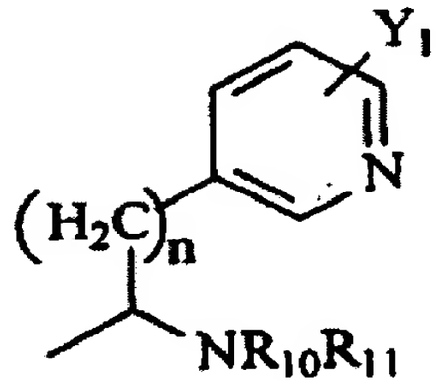

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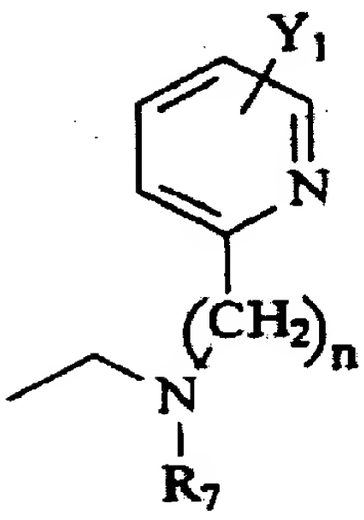

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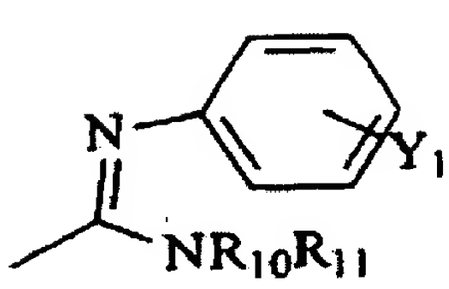
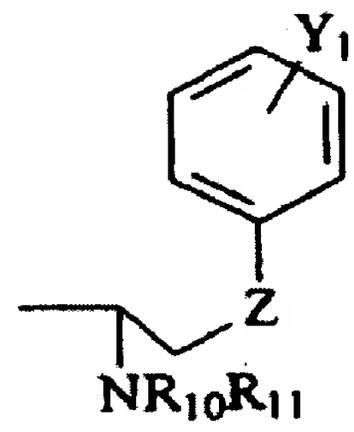
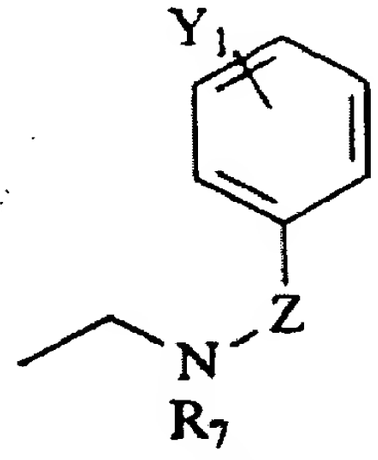


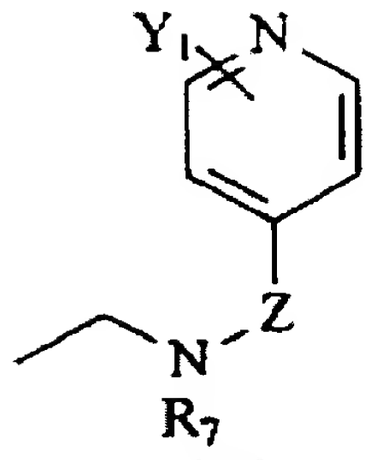
(rr)



(ss)



(tt)



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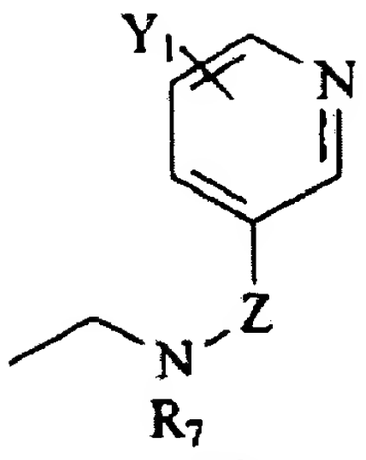
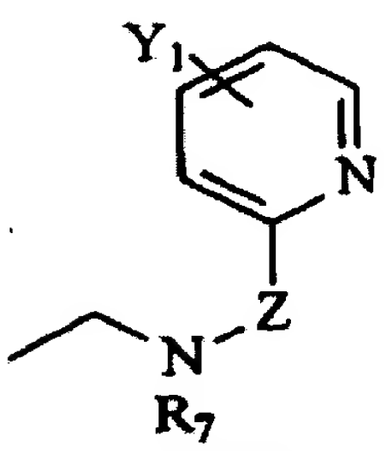


(vv)



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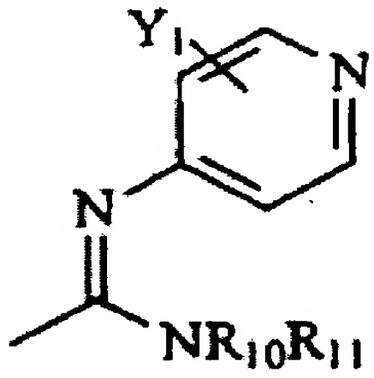

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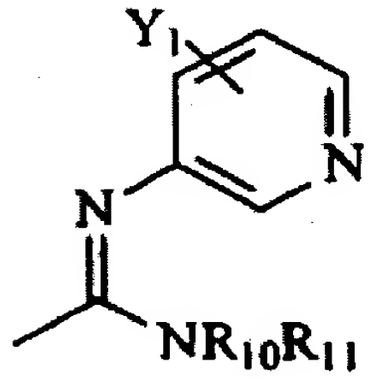

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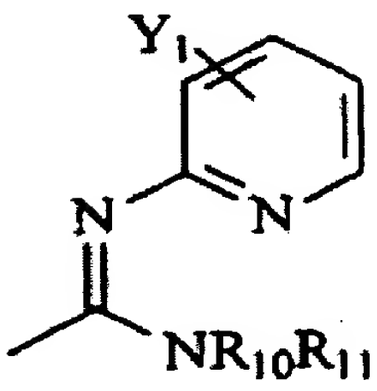

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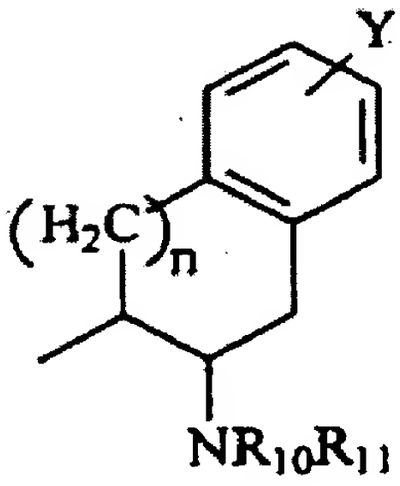
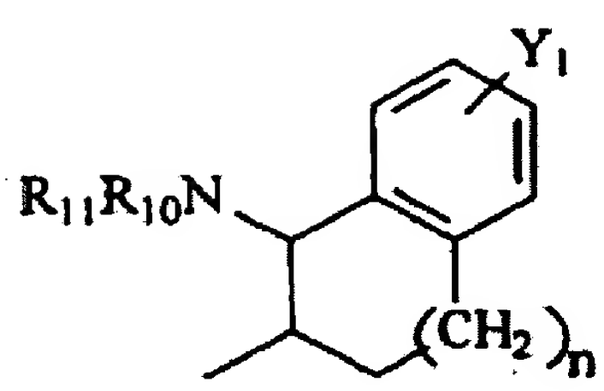


(aaa)



(bbb)

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

X_2 is hydrogen, C_{1-8}alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

or X_1 and X_2 together form =O, =S, or =NH;

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8}alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl

and pharmaceutically acceptable salts thereof.

Claim 8 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein R_1, R_4, R_5, Y_1, Y_2, Z, n, X_1, X_2, and R_7-R_{17} are as in Claim 7;

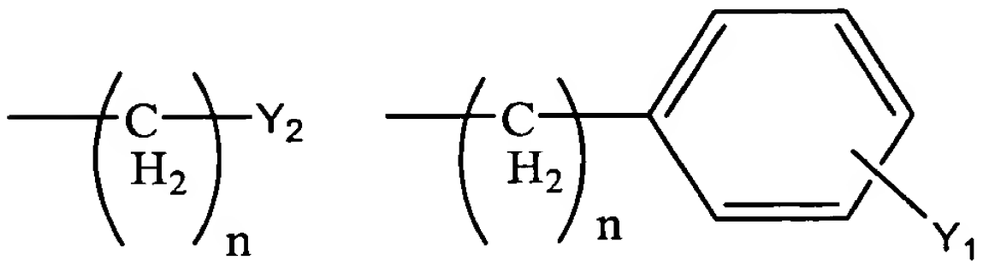
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkynyl, C_{3-8} alkynyl, or CH_2aryl substituted by one or more substituents Y_1; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc).

Claim 9 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1, Y_2, R_4, R_5, Z, n, X_1, X_2 and R_8R_{15} are as in Claim 7;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 10 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1, Z, n, X_1, X_2 and R_8-R_{15} are as in Claim 7;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8}alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 11 (Previously Presented) The kappa opioid receptor antagonist compound of claim 7, wherein Y_1, Z, n, X_1, X_2 and R_8-R_{14} are as in Claim 7;

R_1 is methyl,

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, NHCO2R_{12}, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

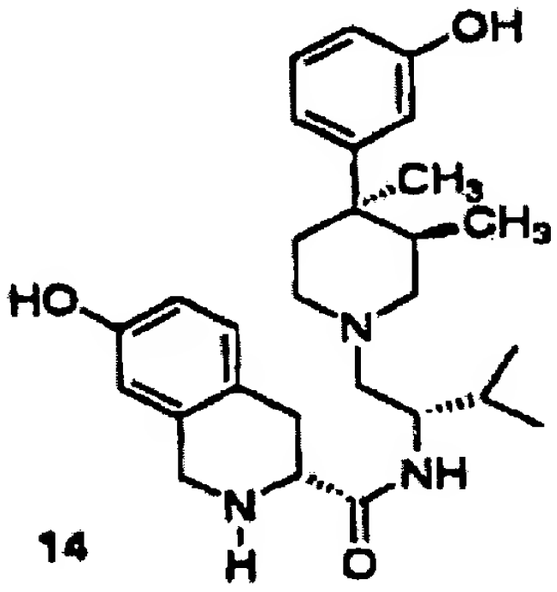
R_4 is C_{1-8} alkyl, or CO_2C_{2-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H;

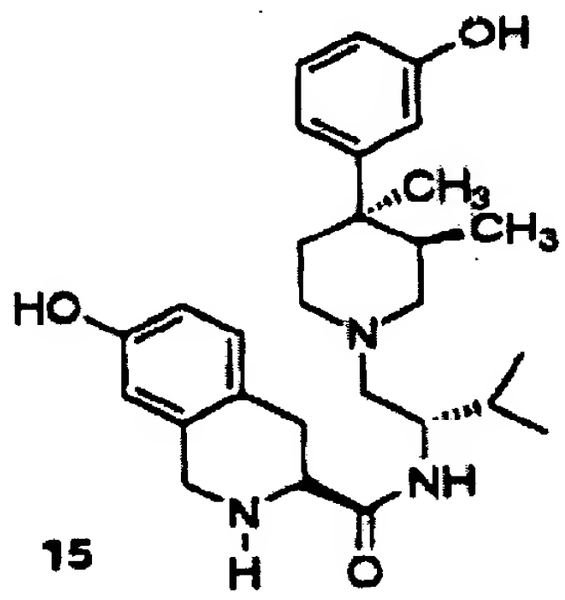
R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, $C_{1\text{-}8}$ alkyl, CH_2aryl substituted by one or more substituents Y_1 or $CH_2(CH_2)_nY_2$.

Claim 12 (Previously Presented) The kappa opioid receptor antagonist of claim 7, wherein said compound is a compound selected from formulae 14-21 as follows:



14



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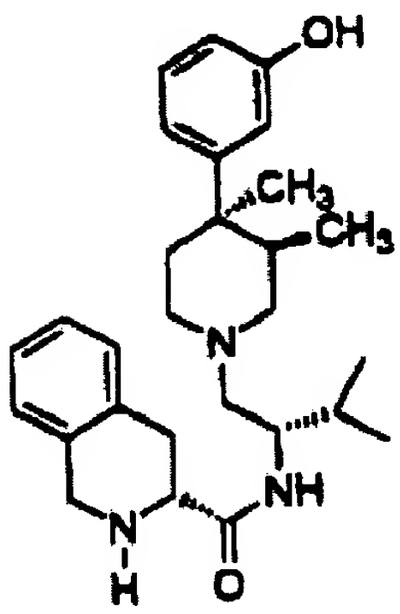
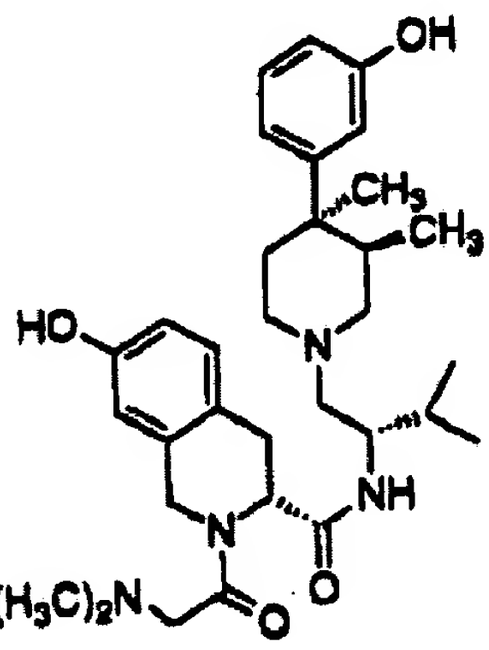
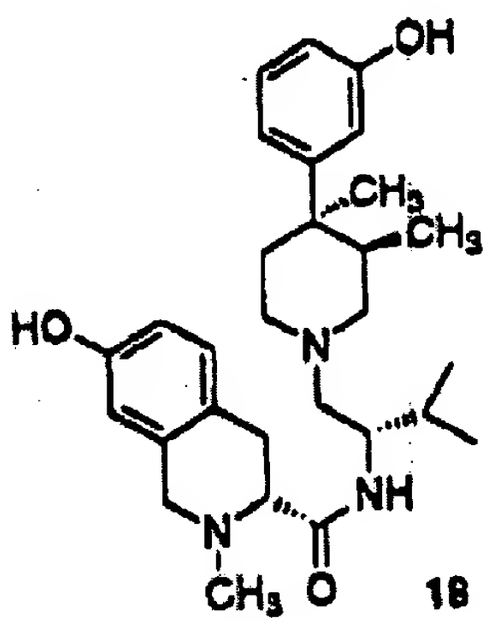


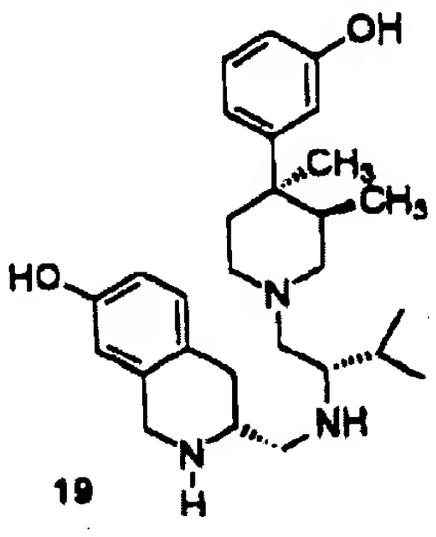
16



17



18



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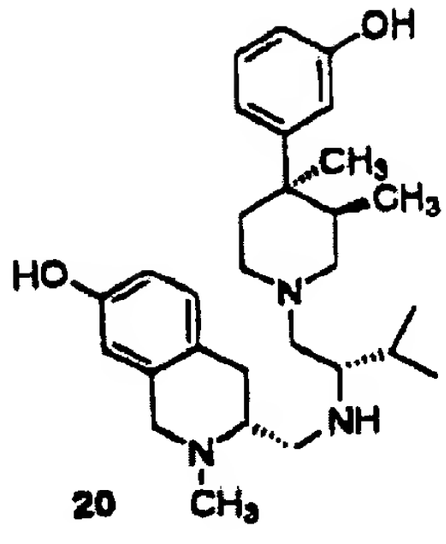
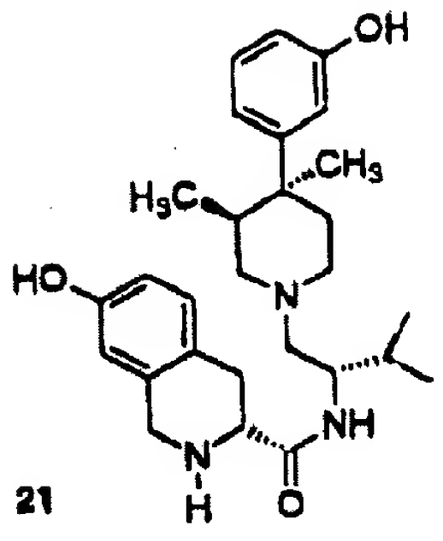


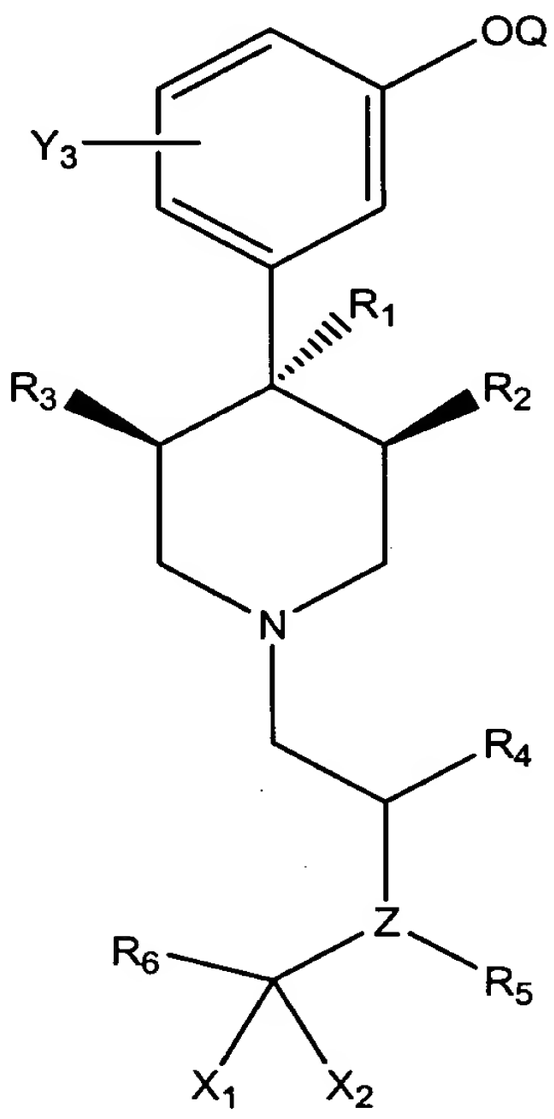
20



21

Claim 13 (Previously Presented) A pharmaceutical composition comprising:

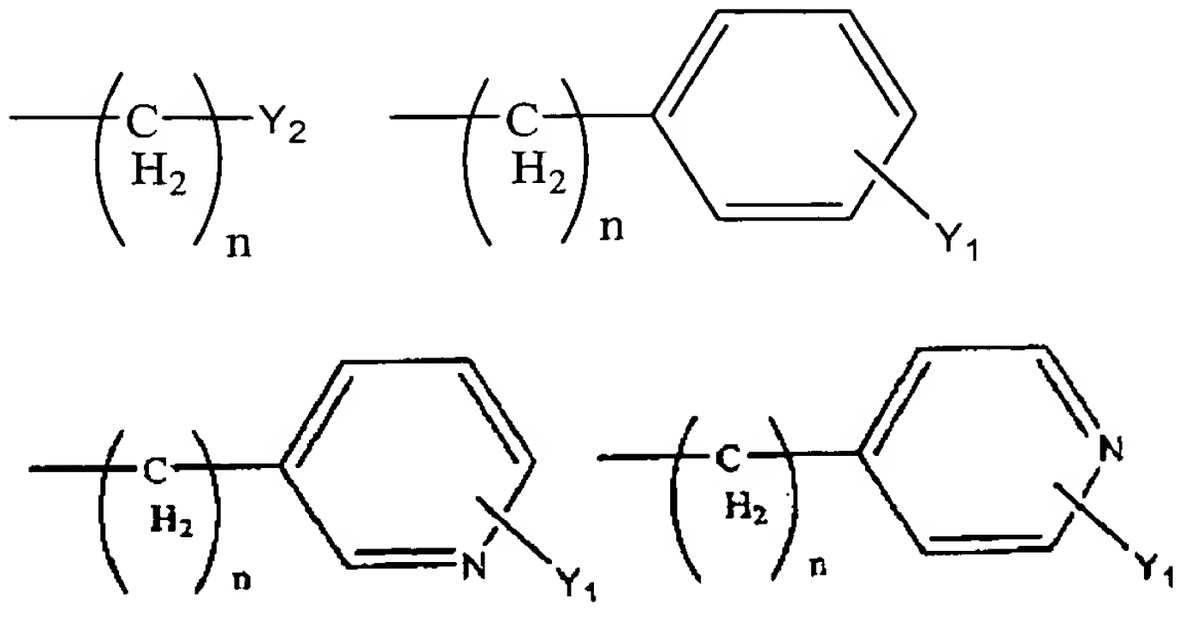
an effective amount of a kappa opioid receptor antagonist and a physiologically acceptable carrier, wherein the kappa opioid receptor antagonist is a compound of formula (I):



(I)

wherein Q is H or COC_{1-8} alkyl;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_1 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, $CO_2R_,$, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH2(CH_2)_nY_2$;

Y_2 is H, CF_3, CO_2R_9, C_{1-6}alkyl, $NR_{10}R11$, $NHCOR_{12}$, $NHCO2R_{12}$, $CONR_3R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, OR_8, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, or $CH_2(CH_2)_nY2$;

R_2 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

R_3 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl or CH_2aryl substituted by one or more groups Y_1;

wherein R_2 and R_3 may be bonded together to form a C_{2-8} alkyl group;

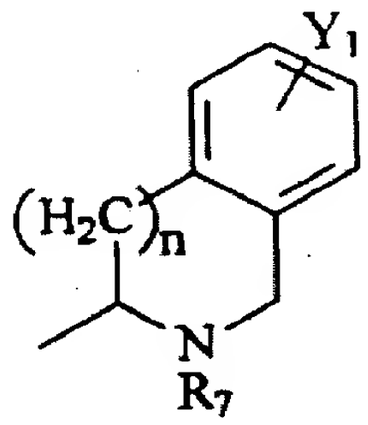
R_4 is hydrogen, C_{1-8} alkyl, CO_2C_{1-8} alkylaryl substituted by one or more groups Y_1, CH_2aryl substituted by one or more groups Y_1, or CO_2C_{1-8} alkyl;

Z is N, O or S; when Z is O or S, there is no R_5

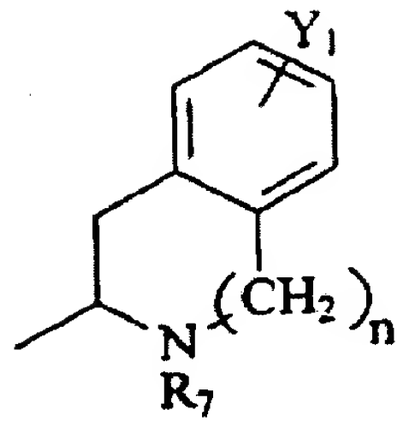
R_5 is H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, $CH_2CO_2C_{1-8}$ alkyl, CO_2C_{1-8} alkyl or CH_2aryl substituted by one or more groups Y_1;

n is 0, 1, 2 or 3;

R_6 is a group selected from the group consisting of structures (a)-(w) and (cc)-(bbb):



(a)



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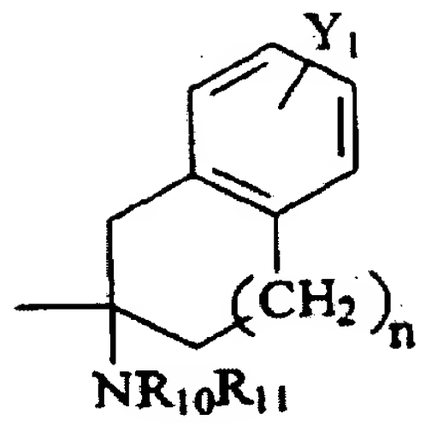

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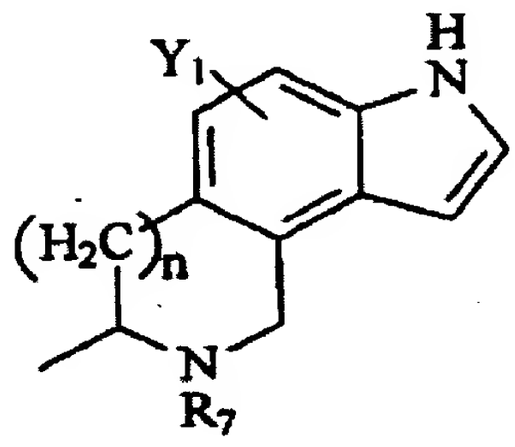

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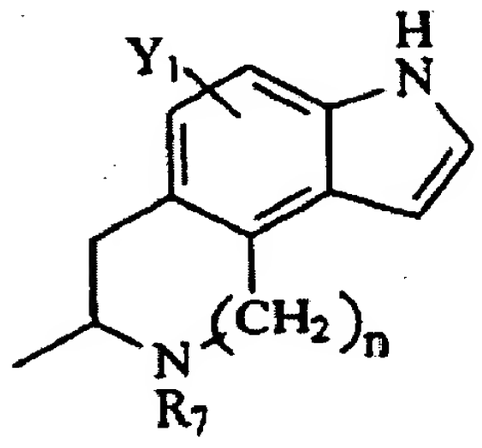

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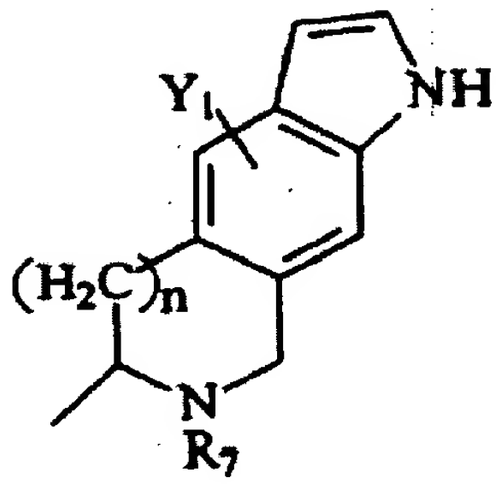

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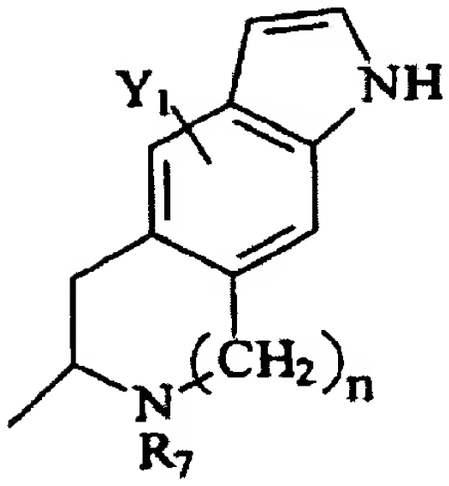

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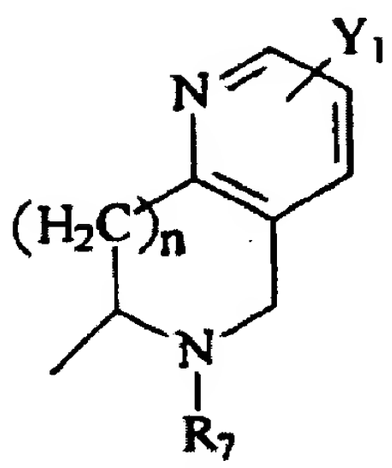

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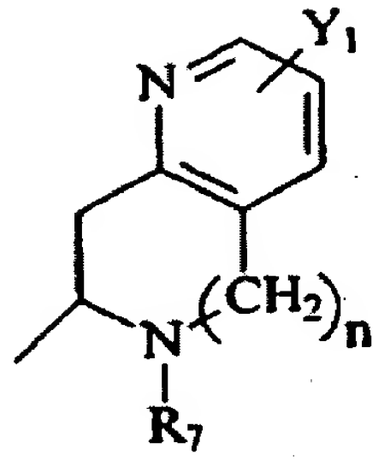

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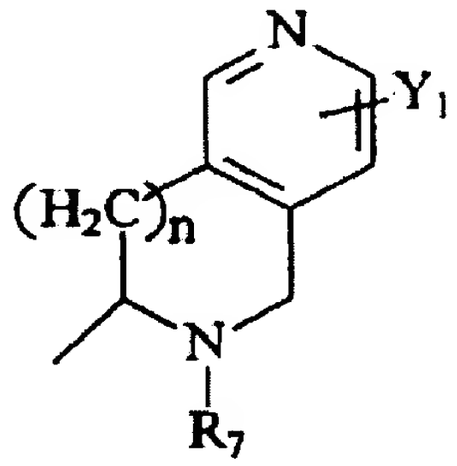

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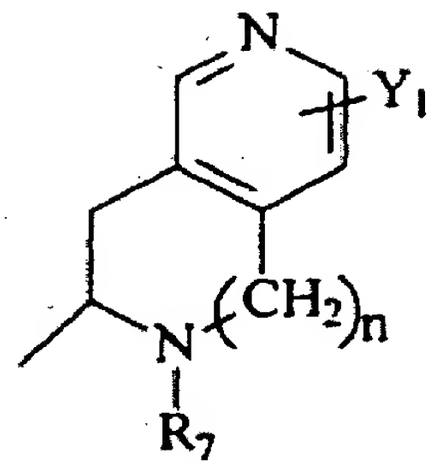

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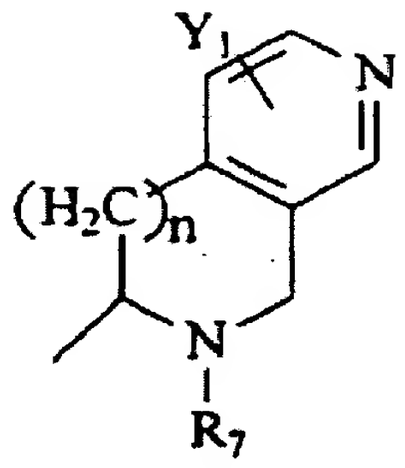

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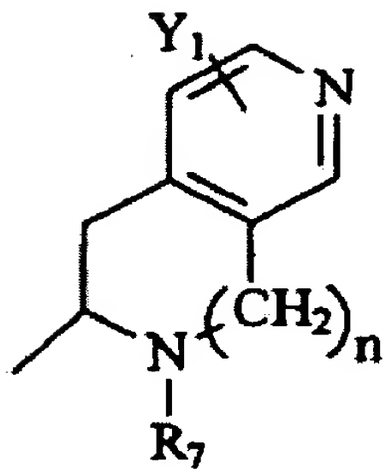

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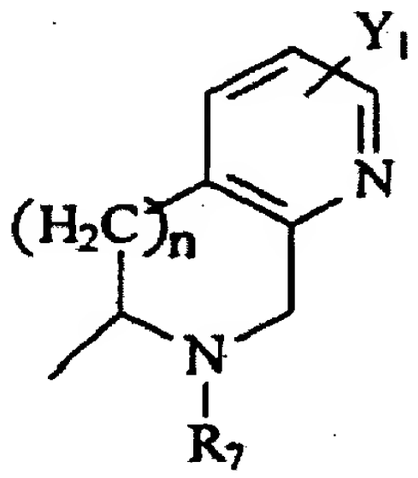

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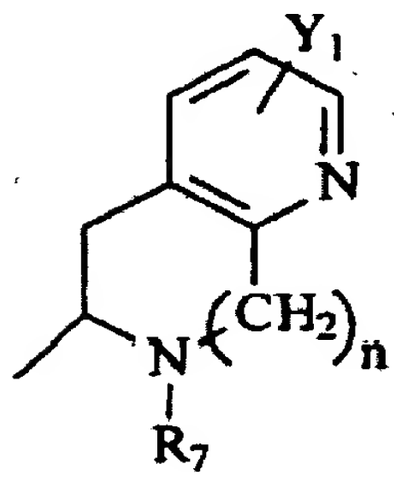

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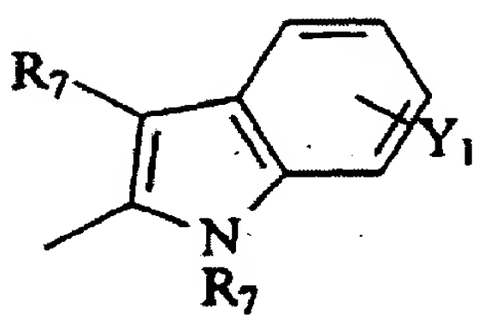

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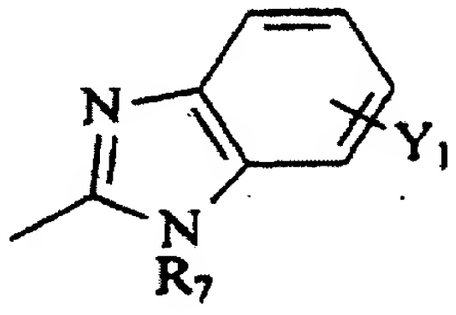

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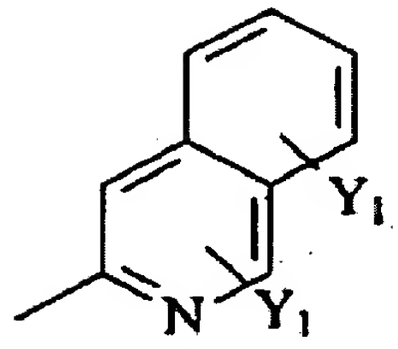
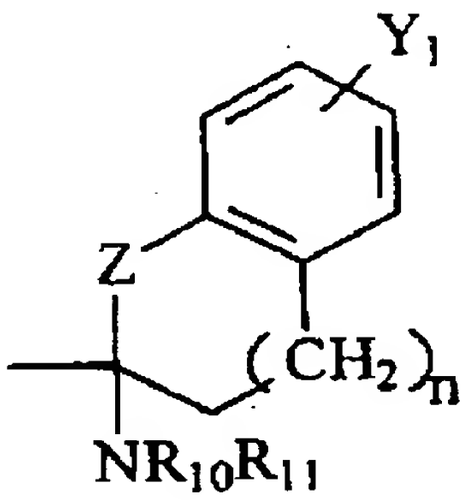
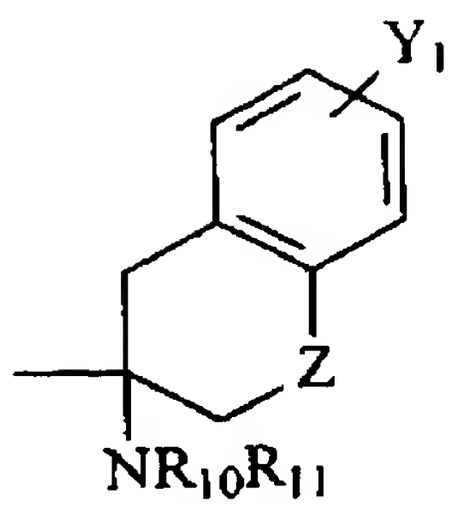


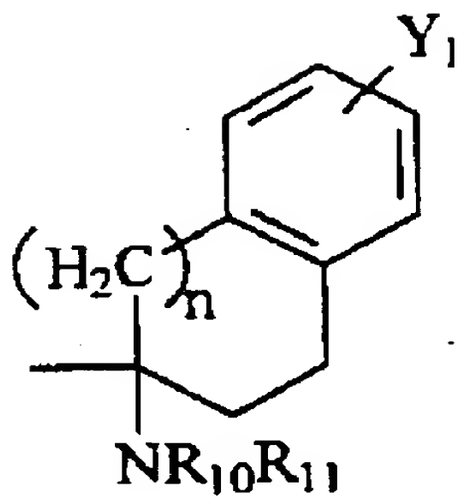
(r)


Y1
Z
(CH2)n
NR10R11

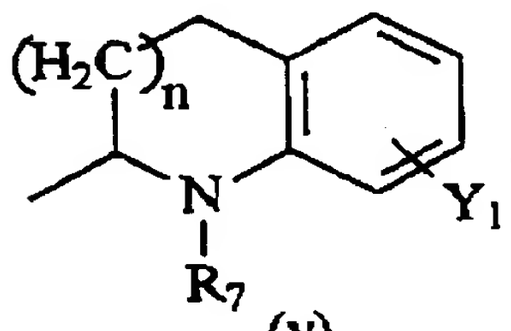
(s)


Y1
Z
NR10R11

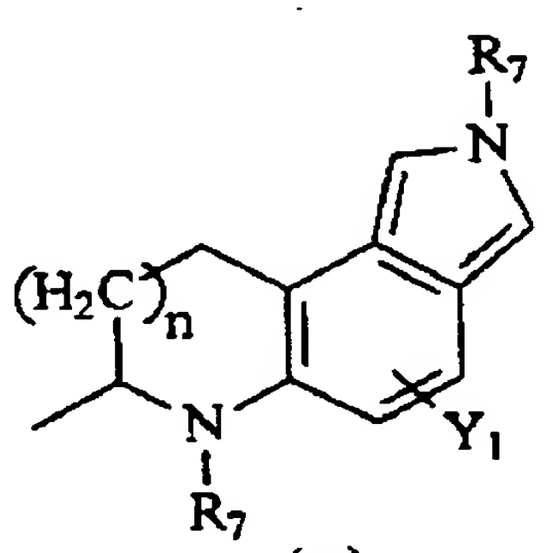
(t)


Y1
(H2C)n
NR10R11

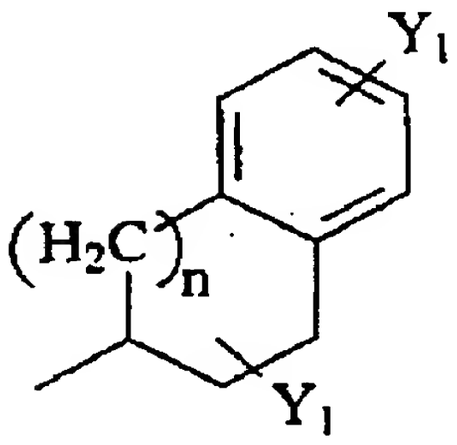
(u)


(H2C)n
N
Y1
R7

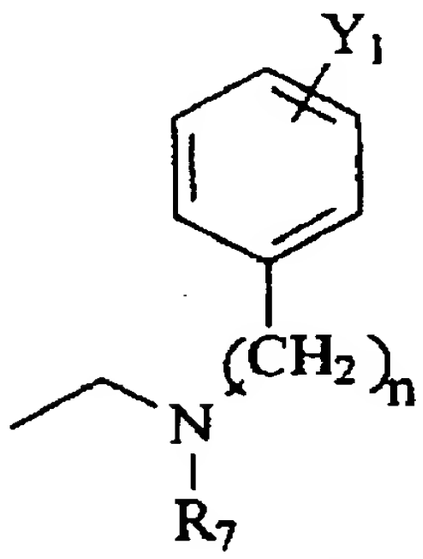
(v)


N
(H2C)n
N
Y1
R7

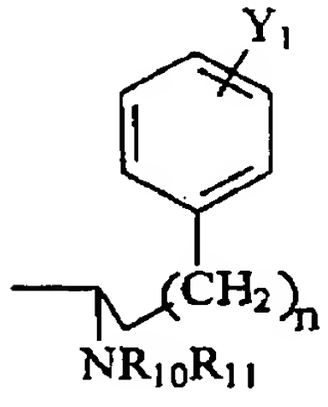
(w)


Y1
(H2C)n
Y1

(cc)


Y1
(CH2)n
N
R7

(dd)



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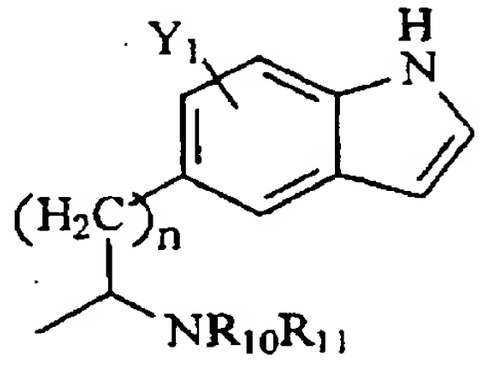

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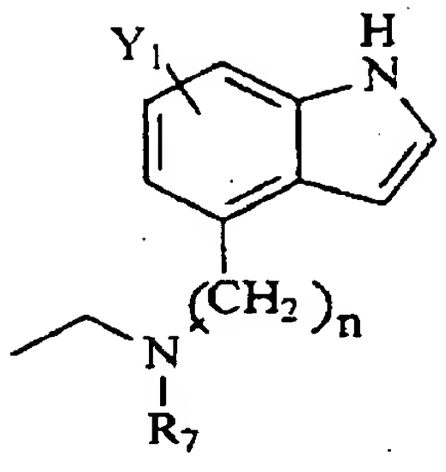

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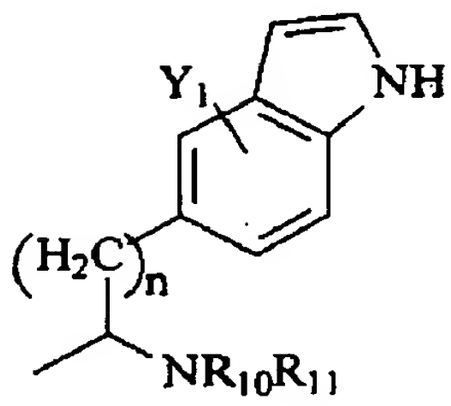

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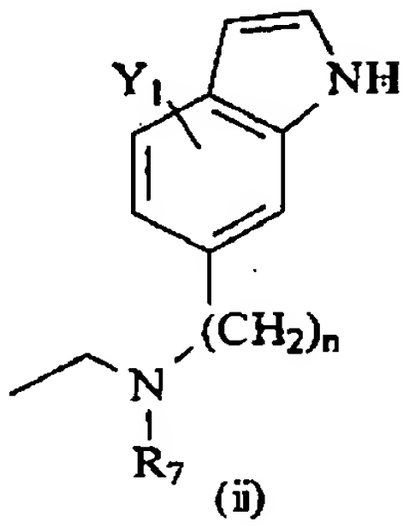

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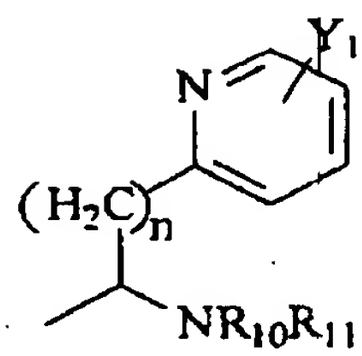

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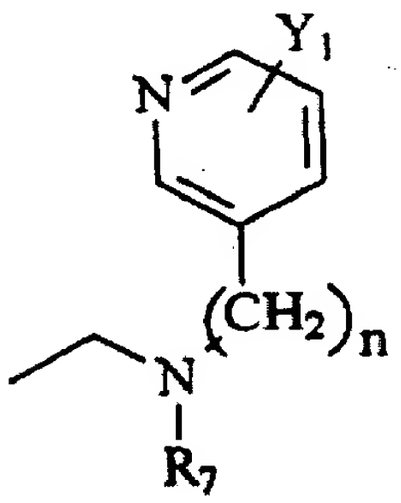

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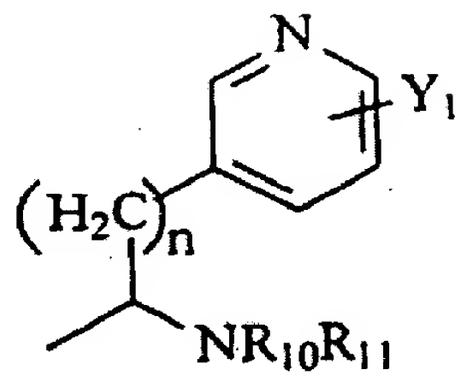

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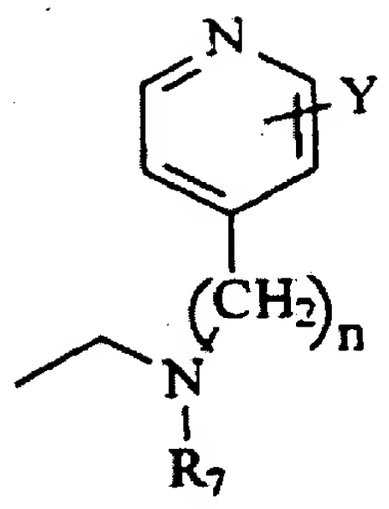

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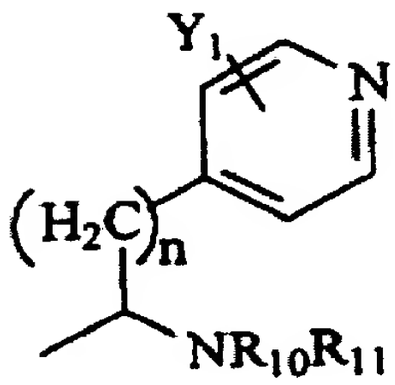

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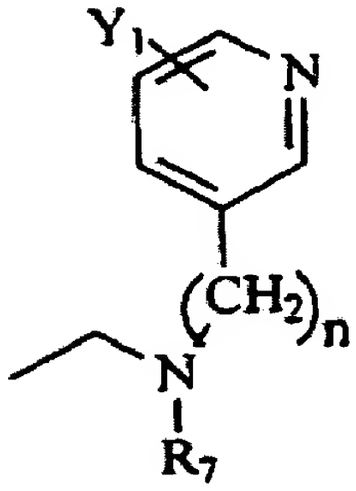

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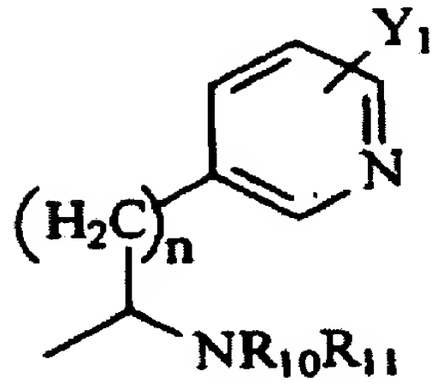

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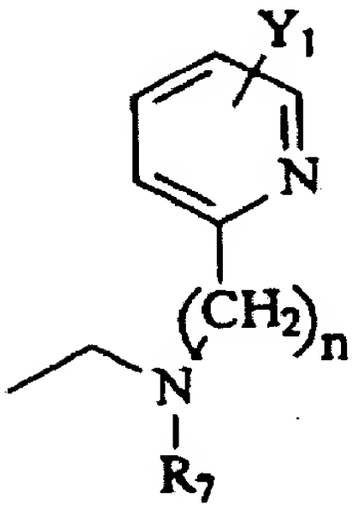

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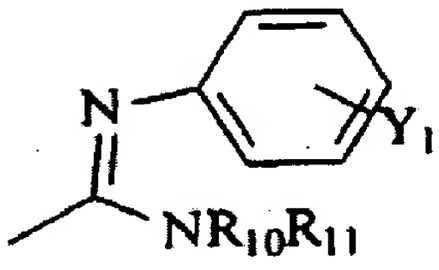

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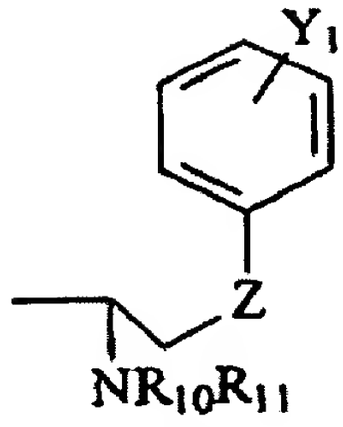

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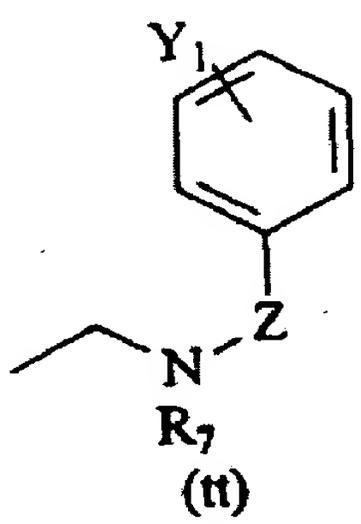

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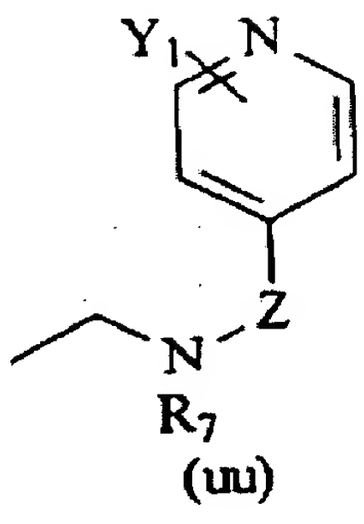

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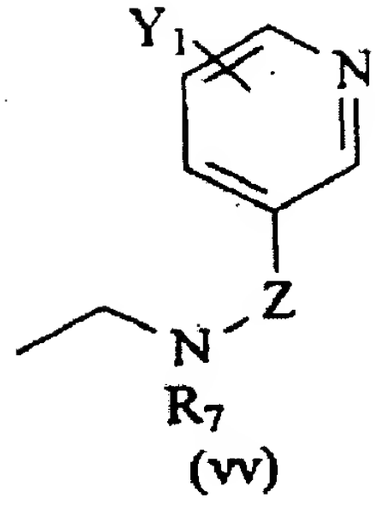

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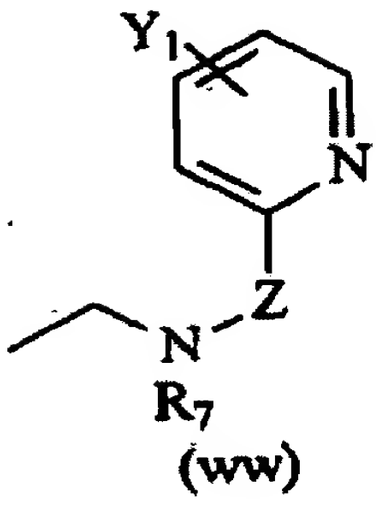

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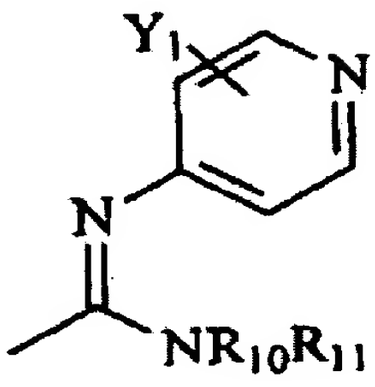

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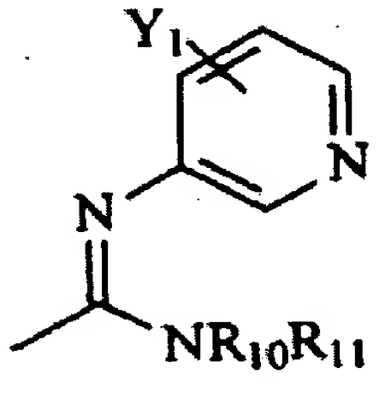

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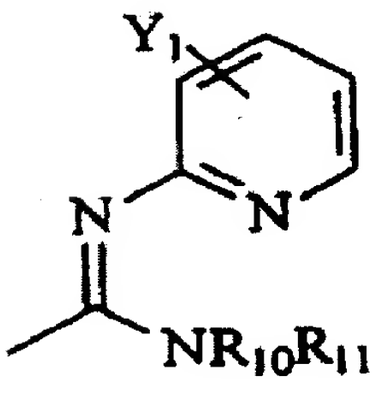

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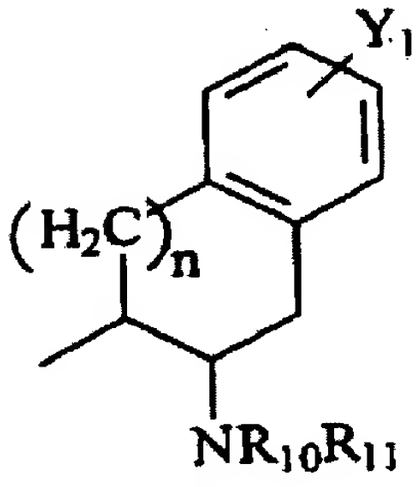

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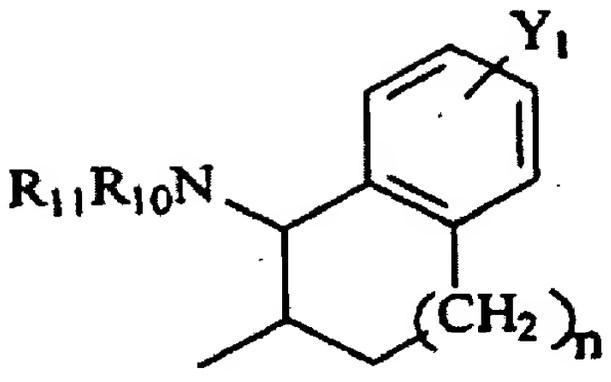


(bbb)

X_1 is hydrogen, C_{1-8} alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

X_2 is hydrogen, C_{1-8}alkyl, C_{3-8}alkenyl, or C_{3-8}alkynyl;

or X_1 and X_2 together form =0, =S, =NH;

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, $CH_2(CH_2)_nY_2$, or $C(=NH)NR_{16}R_{17}$;

R_8 is H, C_{1-8}alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

R_9 is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl;

R_{10} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{11} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{12} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{13} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{14} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{15} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ;

R_{16} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl ; and

R_{17} is H, C_{1-8} alkyl, CH_2 aryl substituted by one or more substituents H, OH, Br, Cl, F, CN, CF_3, NO_2, N_3, C_{1-6} alkyl, or $CH_2(CH_2)_nY_2$'; wherein Y_2' is H, CF_3, or C_{1-6}alkyl

or a pharmaceutically acceptable salt thereof.

Claim 14. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein R_1, R_4, R_5, Y_1, Y_2, Z, n, X_1, X_2, and R_7-R_{17} are as in Claim 13;

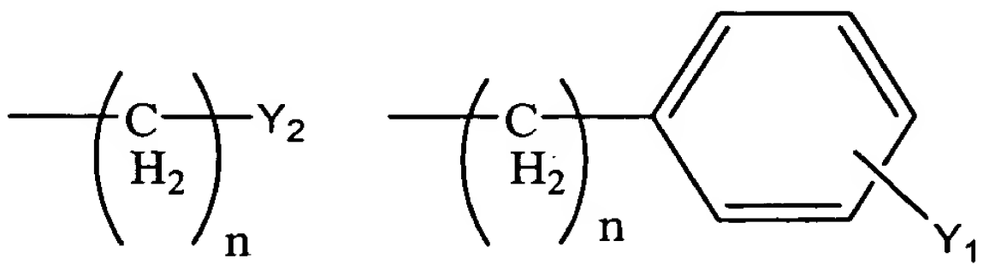
Y_3 is H;

R_2 and R_3 are each, independently, H, C_{1-8} alkyl, C_{3-8} alkenyl, C_{3-8} alkynyl, or CH_2aryl substituted by one or more substituents Y_1; and

R_6 is a group having a formula selected from the group consisting of structures (a)-(w) and (cc).

Claim 15. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y_1, Y_2, R_4, R_5, Z, n, X_1, X_2 and R_8-R_{15} are as in Claim 13;

R_1 is C_{1-8} alkyl, or one of the following structures:



Y_3 is H;

R_2 and R_3 are each, independently, H or C_{1-8} alkyl, wherein R_2 and R_3 cannot both be H at the same time;

R_6 is a formula selected from the structures (a)-(r) shown above; and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 16. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (I), wherein Y_1, Z, n, X_1, X_2 and R_8-R_{15} are as noted- above in Claim 13;

R_1 is C_{1-8} alkyl;

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{12}$, $CONR_{13}R_{14}$, CH_2OH, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each, independently, H or methyl, wherein R_2 and R_3 cannot both be H at the same time;

R_4 is H, C_{1-8} alkyl, CO_2C_{1-8}alkyl, or CH_2 aryl substituted by one or more substituents Y_1 and the stereocenter adjacent to R_4 is in an (S) configuration;

R_5 is H, C_{1-8} alkyl, $CH_2CO_2C_{1-8}$ alkyl;

R_6 is a group having a formula selected from the group consisting of structures (a)-(c) and (h)-(o); and

R_7 is H, C_{1-8}alkyl, CH_2aryl substituted by one or more substituents Y_1, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R_{13}$, $CONR_{14}R_{15}$, or $CH_2(CH_2)_nY_2$.

Claim 17. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound of formula (1), wherein Y_1, Z, n, X_1, X_2 and R_8-R_{14} are as in Claim 13;

R_1 is methyl,

Y_2 is H, CF_3, CO_2R_9, C_{1-6} alkyl, $NR_{10}R_{11}$, $NHCOR_{12}$, $NHCO_2R12$, $CONR_{13}R_{14}$, CH20H, CH_2OR_8, or $COCH_2R_9$;

Y_3 is H;

R_2 and R_3 are each H or methyl, such that when R_2 is H, R_3 is methyl and vice versa;

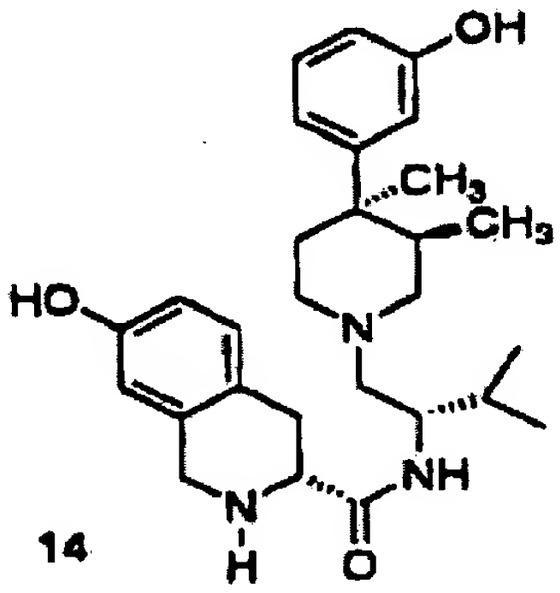
R_4 is C_{1-8} alkyl, or CO_2C_{1-8} alkyl, and the stereocenter adjacent to R_4 has a configuration of (S);

R_5 is H;

R_6 is a group having a formula selected from the group consisting of structures (a) and (b); and

R_7 is H, C_{1-8} alkyl, CH_2aryl substituted by one or more substituents Y, or $CH_2(CH_2)_nY_2$.

Claim 18. (Previously Presented) The pharmaceutical composition of claim 13, wherein said kappa opioid receptor antagonist is a compound selected from formulae 14-21 as follows:



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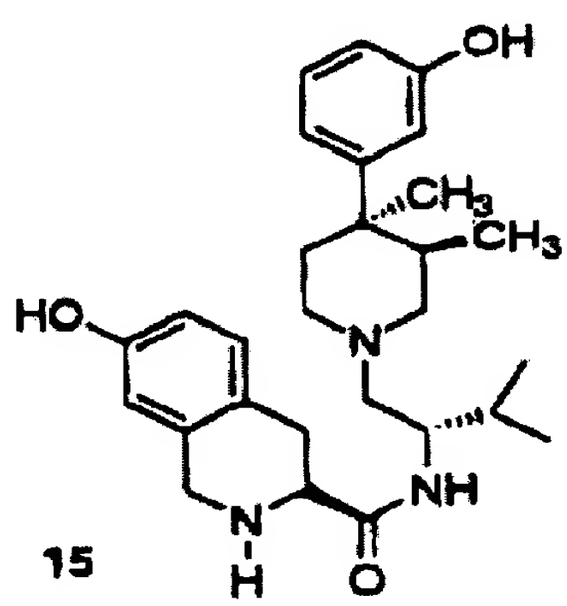

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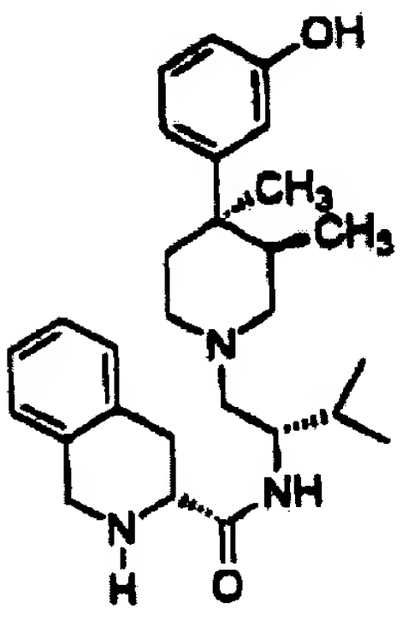

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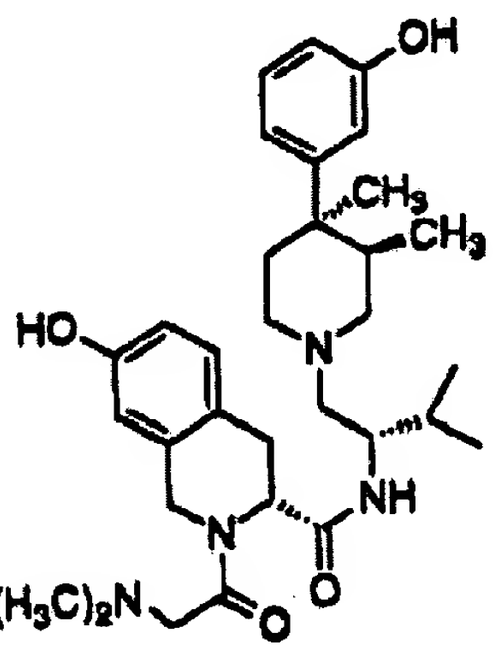

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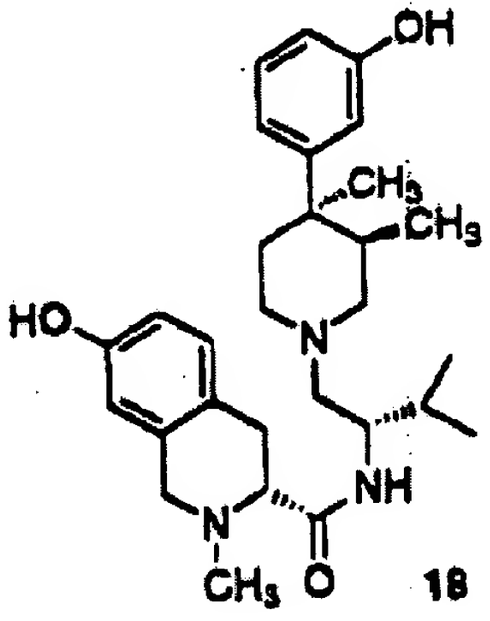

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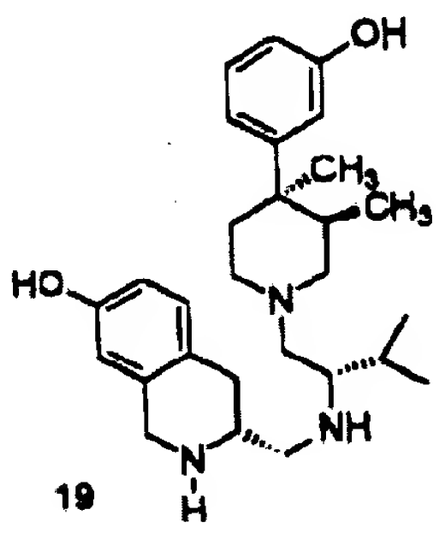

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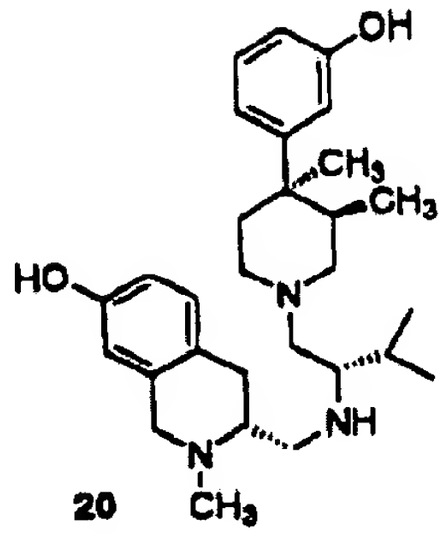

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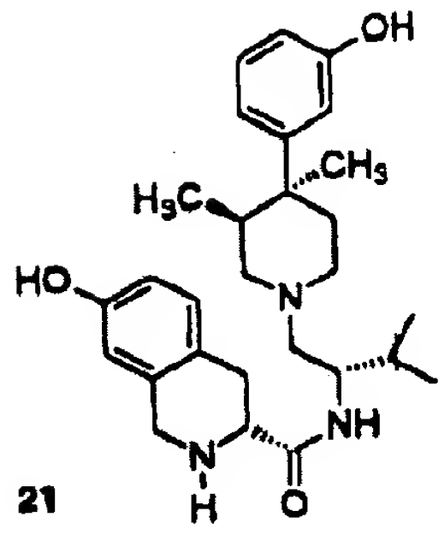

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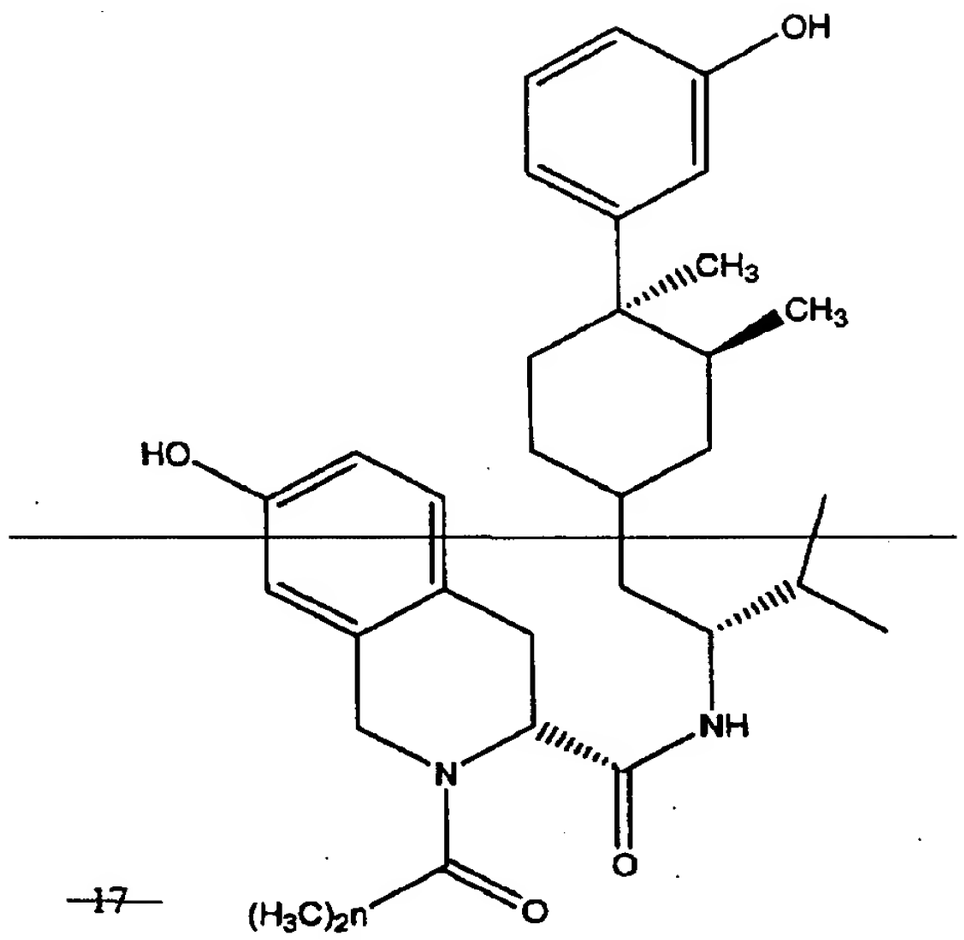
Claim 19. (Original) The pharmaceutical composition of claim 13, wherein said composition is an injectable composition.

Claim 20. (Original) The pharmaceutical composition of claim 13, wherein said composition is an orally administrable composition.

Claim 21. (Original) The pharmaceutical composition of claim 20, wherein said orally administrable composition is in a form selected from the group consisting of tablets, capsules, troches, powders, solutions, dispersions, emulsions and suspensions.

Claim 22. (Currently Amended) The kappa opioid receptor antagonist according to Claim 7, having the chemical formula:



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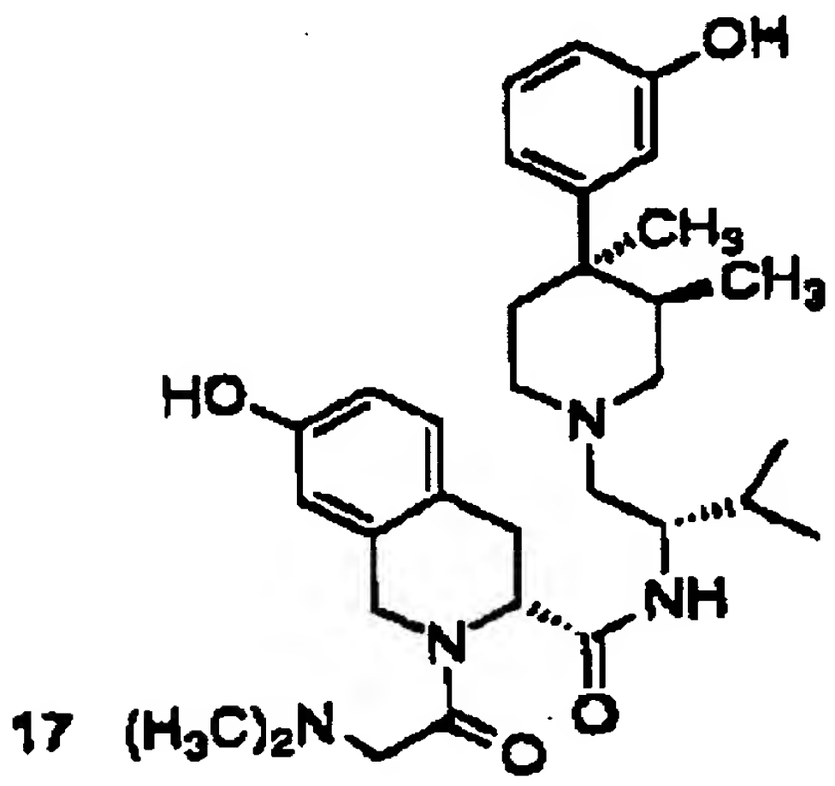

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Claim 23. (Cancelled)

Claim 24. (Cancelled)

Claim 25. (Cancelled)